CHARACTERIZATION OF ADRENAL MASSES WITH CONTRAST ENHANCED CT – WASHOUT STUDY

Dissertation Submitted for

M.D. DEGREE EXAMINATION

In Radio – Diagnosis

BRANCH – VIII

BARNARD INSTITUTE OF RADIOLOGY

MADRAS MEDICAL COLLEGE & RESEARCH INSTITUTE

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI – TAMILNADU

APRIL 2012

MADRAS MEDICAL COLLEGE

1835

CERTIFICATE

This is to certify that **Dr. R.Shankaranandh** has been a post graduate student during the period May 2009 to April 2012 at Barnard Institute of Radiology, Madras Medical College, Rajiv Gandhi Government General Hospital, Chennai. This Dissertation titled **"CHARACTERIZATION OF ADRENAL MASSES WITH CONTRAST ENHANCED CT – WASHOUT STUDY"** is a bonafide work done by him during the study period and is being submitted to the Tamilnadu Dr. M.G.R. Medical University in partial fulfillment of the M.D. Branch VIII Radiodiagnosis Examination to be held in April 2012

PROF.D.RAMESH,
ASSOCIATE PROFESSSOR & GUIDE,,
BARNARD INSTITUTE OF RADIOLOGY,
MADRAS MEDICAL COLLEGE,
RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL
CHENNAI – 600 003

PROF.N.KAILASANATHAN,
HEAD OF THE DEPARTMENT,
BARNARD INSTITUTE OF RADIOLOGY,
MADRAS MEDICAL COLLEGE,
RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL
CHENNAI - 600 003.

PROF.K.VANITHA,
DIRECTOR,
BARNARD INSTITUTE OF RADIOLOGY
MADRAS MEDICAL COLLEGE,
RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL
CHENNAI - 600 003.

PROF.KANAGASABAI, M.D.,
DEAN,
MADRAS MEDICAL COLLEGE,
RAJIV GANDHI GOVERNMENT GENERAL HOSPITAL,
CHENNAI – 600 003

DECLARATION

I **Dr.R.Shankaranandh** solemnly declare that this dissertation entitled, **"CHARACTERIZATION OF ADRENAL MASSES WITH CONTRAST ENHANCED CT– WASHOUT STUDY "** is a bonafide work done by me at the Barnard Institute of Radiology, Madras Medical College and Government General Hospital during the period 2009 – 2011 under the guidance and supervision of the Director, Barnard Institute of Radiology of Madras Medical College and Government General Hospital, Professor **K. Vanitha, M.D., D.M.R.D., D.R.M.,** This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree Radiodiagnosis, Branch VIII.**

Place : Chennai

Date: 28.12.11 **Dr. R.SHANKARANANDH**

ACKNOWLEDGEMENT

I would like to thank **PROF.V.KANAGASABAI, M.D,** Dean, Madras Medical College, Government General Hospital, Chennai, for giving me permission to conduct the study in this institution.

With extreme gratefulness, I express my indebtedness to **Prof. K. VANITHA, M.D., D.M.R.D., D.R.M.,**. Director, Barnard Institute of Radiology, for having encouraged me to take up this study. But for their guiding spirit, perseverance and wisdom, this study would not have been possible.

I express my sincere thanks and gratitude to **Prof.T.S.SWAMINATHAN, M.D., D.M.R.D., F.I.C.R.,** Former Director, Barnard Institute of Radiology for his immense kindness, constant support and consistent encouragement in conducting this study.

I express my sincere thanks and gratitude to **Prof.M.PRABAKARAN, MD, DMRD.**, Former Director, Barnard Institute of Radiology, for having encouraged me to take up this study.

I am deeply indebted to my Head of the Department **Prof. N. KAILASANATHAN M.D.,D.M.R.D.,** whose help, stimulating suggestions and encouragement helped me in the research and writing of this thesis.

I wish to thank **Prof.K.MALATHY, M.D.,D.M.R.D., Prof.A.P.ANNADURAI, M.D.,D.M.R.D.,** and **Prof.K.THAYALAN** for their support, valuable criticisms and encouragement.

I wish to thank my Associate Professors **Dr.S.KALPANA, M.D.,D.M.R.D., Dr.S.BABU PETER, M.D.D.N.B., Dr.D.RAMESH, M.D.,** and Chief Civil Surgeon **Dr.S.SUNDARESWARAN, D.M.R.D.,** for their support, valuable criticisms and encouragement.

I am greatly indebted to my Assistant Professors **Dr.J.DEVIMEENAL, M.D., D.M.R.D., D.N.B., Dr.E.MANIMEKALA, M.D., D.N.B.., Dr.J.CHEZHIAN, M.D., Dr.K. GEETHA, M.D.,** and fellow postgraduates for their untiring help.

Last but not the least, I thank all my patients for their cooperation, without whom this study would not have been possible.

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 04425305301
Fax : 04425363970

CERTIFICATE OF APPROVAL

To
Dr. Dr. R. Shankaranandh
PG in MD Radiodiagnosis
Madras Medical College, Chennai -3

Dear Dr. R. Shankaranandh

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled " A study to characterize adrenal masses with contrast enhanced CT " No. 10092011

The following members of Ethics Committee were present in the meeting held on 27.09.2011 conducted at Madras Medical College, Chennai –3

1. Dr. S.K. Rajan MD	-- Chairperson
2. Dr. V. Kanagasabai MD Dean, Madras Medical College, Chennai -3	-- Deputy Chairman
3. Prof. R. Sundaram MD Vice Principal, Madras Medical College, Chennai -3	-- Member Secretary
4. Prof. R. Nandhini MD Director , Inst. of Pharmacology, MMC , Ch-3	-- Member
5. Prof. Pregna B. Dolia MD Director , Inst. of Biochemistry, M M C, Ch-3	-- Member
6. Thiru . Ulaganathan Administrative Officer, M M C, Ch-3	-- Layperson
7. Thiru. S. Govindasamy BA BL	-- Lawyer
8. Tmt. Arnold Saulina .MA., MSW	-- Social Scientist

We approve the Proposal to be conducted in its presented from

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study , any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics committee

CONTENTS

Introduction

INTRODUCTION

The adrenal gland is a common site of disease, and detection of adrenal masses has increased with the expanding use of cross-sectional imaging. Radiology is playing a critical role in not only the detection of adrenal abnormalities but in characterizing them as benign or malignant.

Abnormalities of the adrenal gland include primary neoplasm, metastases, hemorrhage, or enlargement of the adrenal gland from external hormonal stimulation. Adrenal masses can be divided into two physiologic categories based on whether they hypersecrete a hormone. Hyperfunctioning adrenal masses produce a hormone that results in a chemical imbalance and include pheochromocytomas, aldosteronomas, and cortisol or androgen-producing tumors. Nonfunctioning adrenal masses cause enlargement of the adrenal gland but no significant increased hormone production. Adrenal adenomas and metastases are the most common nonfunctioning adrenal masses.

Adrenal masses are often discovered incidentally and are then termed adrenal incidentalomas. They are discovered many a time after an imaging procedure is performed that is unrelated to the adrenal gland. Usually, the patient has no signs of hormonal excess or obvious underlying malignancy. Less commonly, adrenal Masses are discovered as part of the clinical workup for suspected adrenal disease for example, Cushing syndrome.

The most common lesions, adrenal metastases and adenomas cannot be characterized so easily. This is usually because they are small, without specific diagnostic features, and frequently appear similar to each other when detected. The usual imaging dilemma is therefore to differentiate between these two very different lesions. The diagnosis has profound consequences for the patient.

In a patient with an extraadrenal malignancy, the determination that an adrenal mass is metastatic often means the primary disease is incurable and palliative therapy is instituted. On the other hand, characterizing a lesion as benign in these circumstances potentially permits curative therapy for the primary disease.

CHARACTERIZATION OF ADRENAL MASSES WITH CONTRAST ENHANCED CT

CT:

Most adrenal lesions are detected by CT, usually contrast-enhanced CT. Most benign and malignant lesions show variable enhancement on dynamic contrast-enhanced CT. They can rarely be characterized by this test alone.

There may be some imaging clues that permit early characterization such as significant interval growth, large size, and markedly irregular lesion. But the macroscopic features for the majority of lesions do not usually permit an easy diagnosis. Most benign and malignant lesions have very similar macroscopic appearances when detected. This is because they are generally small and homogeneous.

A few may be confidently assigned as benign. These include cysts which show water density and myelolipomas, which usually contain macroscopic fat. So indeterminate lesions are those that are usually of moderate size (1–3 cm), homogeneous, and smooth walled.

A dynamic contrast-enhanced CT cannot, on its own, characterize most of these lesions.

But it has been known that unenhanced CT can be useful in differentiating benign from malignant disease. Most benign adenomatous lesions show a relatively low density on unenhanced CT because of the abundant presence of intracellular fat. Most malignant lesions are lipid-poor and show higher attenuation values.

It is possible to choose an attenuation threshold that effectively differentiates most adenomas from malignant adrenal lesions [2]. An adrenal lesion measuring ≤ 10 HU is almost always benign. Unfortunately, only 70% of adenomas are lipid-rich, 30% being lipid poor, meaning that many lesions cannot be differentiated from metastases by this test.

The ability to differentiate most lipid-rich benign lesions from indeterminate lipid-poor lesions has stood the test of time. Therefore the next suitable test is unenhanced CT.

The placement of the region of interest (ROI) for density measurement is crucial for accurate adrenal characterization. The ROI should be at least one half to two thirds of the adrenal surface area. Otherwise noise effects from small ROIs will render the measurement inaccurate.

Enhanced and Delayed Contrast-Enhanced CT

Enhanced contrast-enhanced CT alone is not of much help to characterize an adrenal lesion. But delayed contrast-enhanced CT along with the enhanced study, enables characterization of most lipid-rich and lipid-poor adrenal lesions.

This is advantageous because almost all adrenal lesions can be differentiated by CT. And CT is faster, cheaper, and more available than MRI. Modern MDCT dose reduction programs render the test suitable for most patients with indeterminate adrenal incidentalomas

Circulating contrast material within the adrenal gland that had previously been injected IV on dynamic contrast-enhanced CT tends to washout from adenomatous lesions far quicker than nonadenomatous lesions, particularly malignant lesions.

If attenuation measurements of the adrenal gland were made on images performed 15 minutes after the contrast-enhanced CT, an attenuation threshold could be found in the delayed scan. The ability of the delayed scan alone to differentiate benign from malignant lesions found difficulty due to considerable overlap between adenomas and non adenomas. Further, delayed CT densitometry measurements depends on the type, total dose, and injection rate of intravenous contrast material, as well as the cardiac output of the patient, an absolute attenuation measurement on a delayed scan was not found to be very useful.

Thus test sensitivity and specificity are suboptimal because the absolute attenuation values in enhanced and delayed scans of lipid-poor adrenal adenomas tended match that of lipid poor malignant lesions.

However, the fraction of contrast material that washed out of the adrenal gland from the enhanced to the delayed contrast-enhanced CT, helps characterize most adenomatous lesions. Thus, both lipid-rich and lipid-poor adenomatous lesions can be characterized with this single test.

If lesions show an absolute contrast-enhanced percentage washout—the fraction of the difference between the enhanced and delayed contrast-enhanced CT divided by the absolute enhancement (the increase in adrenal attenuation from unenhanced CT to enhanced contrast-enhanced CT)—of greater than 60%, then lesions are assumed to be benign.

A relative contrast- enhanced percentage washout is also calculated, and a value of 40% or greater is used. This is calculated by assigning the unenhanced CT lesion attenuation value as zero and calculating the fraction using the same numerator as absolute contrast-enhanced percentage washout, but the denominator of the contrast-enhanced CT attenuation value alone.

Lesions showing an absolute contrast-enhanced percentage washout and relative contrast-enhanced percentage washout of less than 60% and 40%, respectively, are consistent with non adenomatous lesions, usually metastases.

The absolute contrast-enhanced percentage washout and relative contrast-enhanced percentage washout test accuracy using 10-minute delayed contrast-enhanced CT has also been calculated and found to be highly accurate.

But use of the 15-minute delayed image it is recommended as standard for this adrenal CT protocol to calculate the fractional washout.

It has been proposed that Relative Percent Washout and Absolute Percent Washout tests are so effective for differentiating adenomas from nonadenomas that other imaging tests (including MR and PET) should only be needed in unusual circumstances

IMAGING ALGORITHM

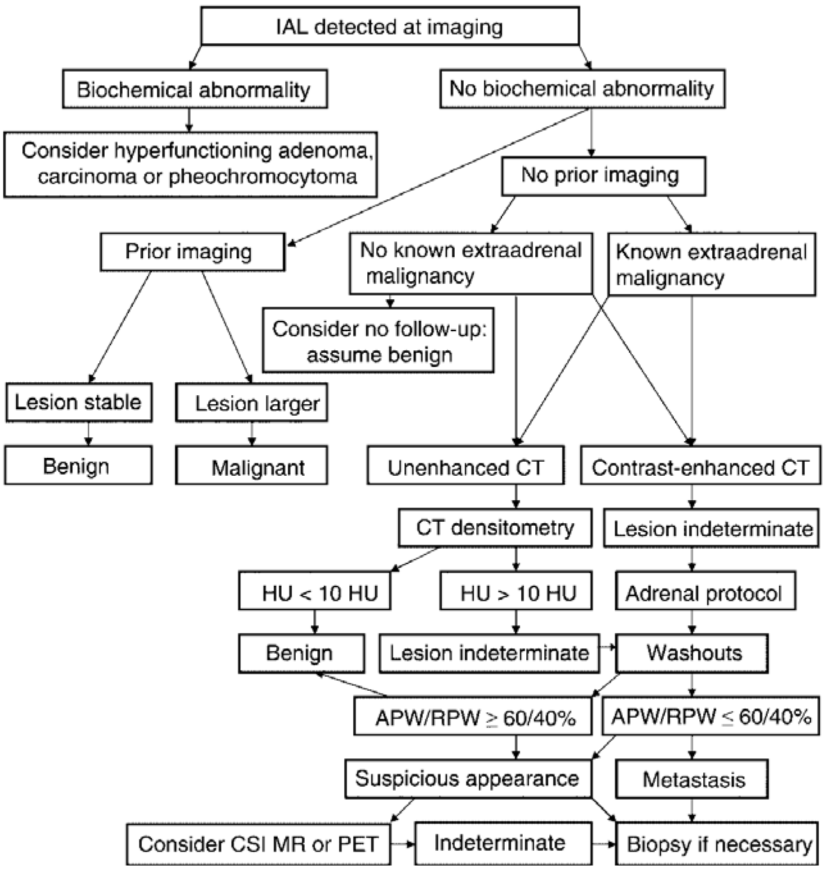


Figure 5

Aim of the Study

AIM OF THE STUDY

To assess the accuracy of Contrast Enhanced CT - Washout study in characterizing adrenal masses as benign or malignant, i.e as adenomas or non adenomas.

Relevant Anatomy and Physiology

ANATOMY AND PHYSIOLOGY OF ADRENAL GLANDS

Anatomically, the adrenal glands are located in the retroperitoneum superior to the kidneys, bilaterally. They are surrounded by an adipose capsule and renal fascia. They are found at the level of the 12th thoracic vertebra. Each adrenal gland has two distinct structures, the outer adrenal cortex and the inner medulla, both of which produce hormones. The cortex mainly produces cortisol, aldosterone and androgens, while the medulla chiefly produces epinephrine and norepinephrine. The combined weight of the adrenal glands in an adult human ranges from 7 to 10 grams.

Adrenal Gland Anatomy

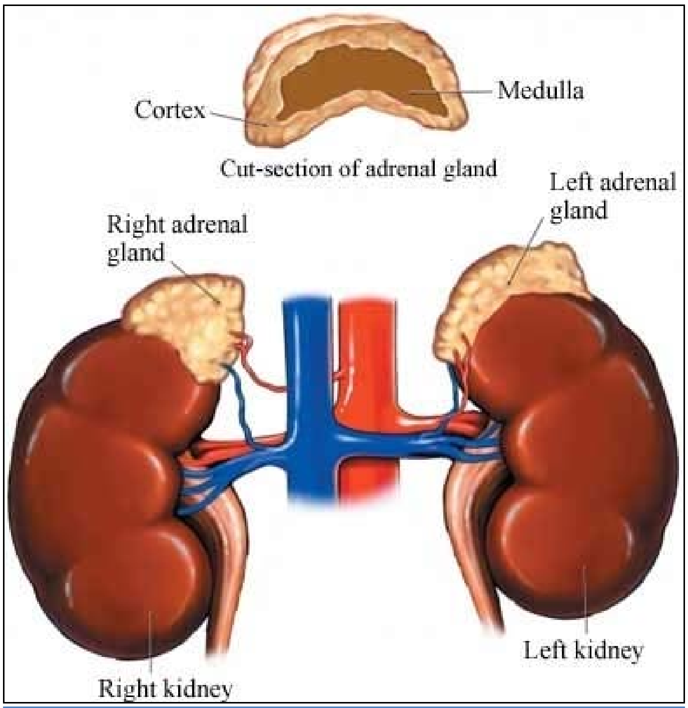


Figure 1

CORTEX

The adrenal cortex is devoted to the synthesis of corticosteroid and androgen hormones. In contrast to the direct innervation of the medulla, the cortex is regulated by neuroendocrine hormones secreted from the pituitary gland which are under the control of the hypothalamus, as well as by the renin-angiotensin system.

The adrenal cortex comprises three zones, or layers.

Zona glomerulosa

The outermost layer, the zona glomerulosa is the main site for production of mineralocorticoids, mainly aldosterone, which is largely responsible for the long-term regulation of blood pressure.

Zona fasciculata

Situated between the glomerulosa and reticularis, the zona fasciculata is responsible for producing glucocorticoids, such as 11-deoxycorticosterone, corticosterone, and cortisol in humans. Cortisol is the main glucocorticoid.

Zona reticularis

The inner most cortical layer, the zona reticularis produces androgens, mainly dehydroepiandrosterone (DHEA) DHEA sulfate (DHEA-S), and androstenedione (the precursor to testosterone) in humans.

MEDULLA

The adrenal medulla is the core of the adrenal gland, and is surrounded by the adrenal cortex. It secretes approximately 20% norepinephrine and 80% epinephrine. These are the major hormones underlying the fight-or-flight response.

Adrenal Gland Schematic section and Histology

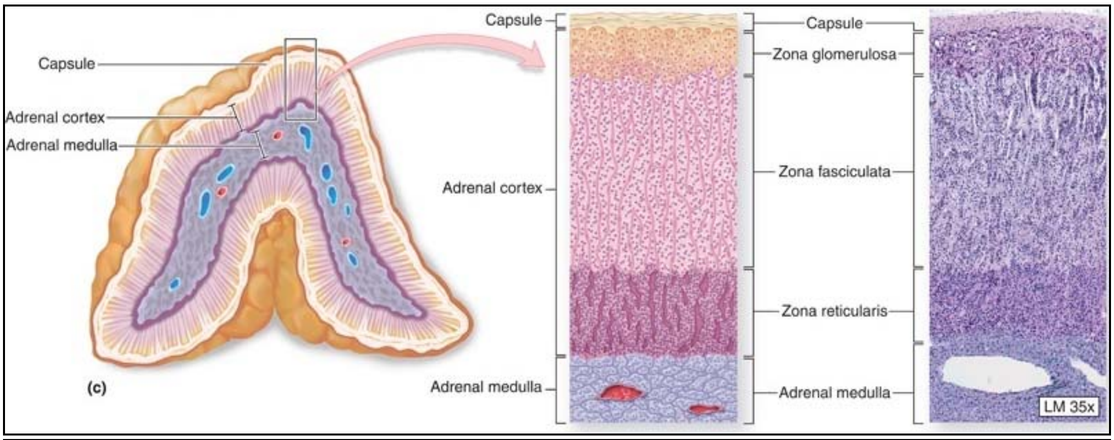


Figure 2

Blood supply

There are usually three arteries that supply each adrenal gland:

The superior suprarenal artery is provided by the inferior phrenic artery. The middle suprarenal artery is provided by the abdominal aorta. The inferior suprarenal artery is provided by the renal artery.

Venous drainage of the adrenal glands is achieved via the suprarenal veins:

The right suprarenal vein drains into the inferior vena cava. The left suprarenal vein drains into the left renal vein or the left inferior phrenic vein.

The adrenal glands and the thyroid gland are the organs that have the greatest blood supply per gram of tissue. Up to 60 arterioles may enter each adrenal gland. This may be one of the reasons lung cancer commonly metastasizes to the adrenals.

NORMAL CT ANATOMY

At CT, the adrenal glands appear as triangular or crescentic soft tissue structures draped over the upper poles of the kidneys immediately anterolateral to the crura of the diaphragm. The two limbs of each adrenal gland appear as thin strands that join superiorly.

Normal CT axial sectional Anatomy

Figure 3

The right adrenal gland is located in an area just superior to the right kidney, medial to the right lobe of the liver, lateral to the crus of the right hemidiaphragm, and posterior to the inferior vena cava. Its shape is variable but may resemble an elongated comma lying in the crease between the liver and the crus of the diaphragm. It also may be shaped like an inverted letter V or Y. The lateral limb of the adrenal gland lies close to the right lobe of the liver and can sometimes be difficult to separate from the surface of the liver.

The left adrenal gland is located superior to and extends anterior to the upper pole of the left kidney in a triangle formed by the left lateral margin of the aorta, the posterior surface of the body and tail of the pancreas, and the anterior superior medial surface of the upper pole of the left kidney. It can be shaped like an inverted letter V or Y, an inverted or reversed letter L, or it may be triangular.

Coronal CT Anatomy

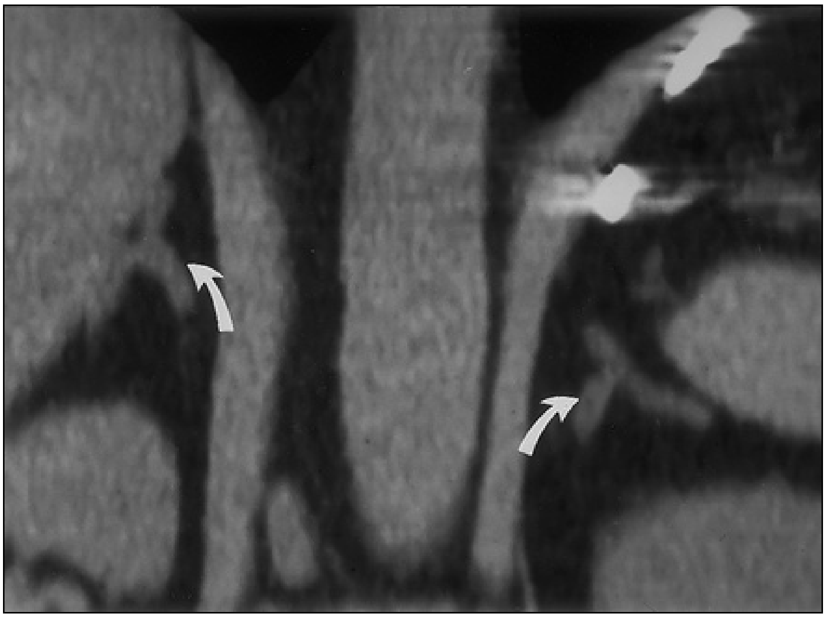


Figure 4

Coronal reformatted image from helical CT data shows the triangular shape of the adrenal gland (arrows) and its relationship to the kidneys and diaphragm

Review of Literature

REVIEW OF LITERATURE

Melvyn Korobkin and Frederick . J Brodeur et al studied contrast enhancement washout curves of 52 adenomas and 24 non adenomas. The optimal threshold value and the corresponding sensitivity and specificity were calculated for the diagnosis of adenoma. Also the absolute and relative percentage washouts were calculated at time delays from 5 to 45 minutes after contrast enhancement.

The mean percentage enhancement washout for adenomas was 51% at 5 minutes and 70% at 15 minutes, compared with 8% and 20% respectively for non adenomas. The sensitivity and specificity of diagnosing adenomas was higher at the 15 minute scan than at the 5 minute delayed scan. Based on the 15 minute delayed scan's calculation of percentage enhancement washout with 60 HU as threshold, there was a sensitivity of 88% and specificity of 96%. For the relative percentage washout with a 37HU threshold, the sensitivity and specificity both were 96%.

Elaine M. Caoili, MD et al evaluated One hundred sixty-six adrenal masses were evaluated with a protocol consisting of unenhanced CT, and, for those with attenuation values greater than 10 HU, contrast material–enhanced and delayed enhanced CT. Attenuation values and enhancement washout calculations were obtained. An adenoma was diagnosed if a mass had an attenuation value of 10 HU or less at unenhanced CT or a percentage enhancement washout value of 60% or higher.

The final diagnosis was adenoma in 127 masses and nonadenoma in 39. Masses measuring more than 10 HU on unenhanced CT scans were confirmed at biopsy (*n* _ 28) or were examined for stability or change in size at follow-up CT performed at a minimum interval of 6 months (*n* _ 33). Thirty-six (92%) of 39 nonadenomas and 124 (98%) of 127 adenomas were correctly characterized. The sensitivity and specificity of this protocol were 98% and 92%, respectively. This protocol correctly characterized 160 (96%) of 166 masses. The study concluded that With a combination of unenhanced and delayed enhanced CT, nearly all adrenal masses can be correctly categorized as adenomas or nonadenomas.

Giles W. L.Boland et al analyzed ten CT reports, from which individual adrenal lesion density measurements were obtained for 495 adrenal lesions (272 benign lesions and 223 malignant lesions). Threshold analysis generated a range of sensitivities and specificities for lesion characterization at different density thresholds. The study found that sensitivity for characterizing a lesion as benign ranged from 47% at a threshold of 2 H to 88% at a threshold of 20 H. Similarly, specificity varied from 100% at a threshld of 2 H to 84% at a threshold of 20 H. It was concluded that the attempt to be absolutely certain that an adrenal lesion is benign may lead to an unacceptably low sensitivity for lesion characterization. The threshold chosen will depend on the patient population and the cost benefit approach to patient care.

Song et al. study showed that in 973 consecutive patients with 1,049 incidental adrenal masses adenomas accounted for 75% of incidental masses, of which 78% were lipid rich adenomas with native CT attenuation values of less than 10 HU.

Lee et al. first reported that unenhanced CT densitometry could effectively differentiate many adrenal adenomas from nonadenomatous disease. They found that the mean attenuation of adenomas (−2.2 HU) was significantly lower than that of nonadenomas (28.9 HU). By using a threshold of 0 HU, these lesions could be then differentiated with sensitivity and specificity of 47% and 100%, respectively.

Blake et al. study showed that an unenhanced CT attenuation value of 0 HU or lower should supersede the contrast washout characteristics and that noncalcified, nonhemorrhagic adrenal lesions with a native density of 43 HU or more should be considered indeterminate and suspicious for malignancy irrespective of their contrast washout characteristics.

Elaine M. Caoili1 and Melvyn Korobkin et al studied eighteen proven lipid-poor adenomas, 56 lipid-rich adenomas, and 40 adrenal nonadenomas. They underwent CT before, immediately after, and 15 min delay after IV contrast injection.

The mean unenhanced value of the lipid-poor adenomas was significantly higher than that of the lipid-rich adenomas ($p < 0.001$) but was not significantly different from the value of the nonadenomas ($p = 0.24$). The mean enhanced attenuation value of the lipid-poor adenomas was significantly higher than that of the lipid-rich adenomas ($p < 0.01$) but was not significantly different from that of the nonadenomas ($p = 0.03$). The mean delayed contrast-enhanced attenuation value of the lipid-poor adenomas was significantly higher than that of the lipid-rich adenomas ($p < 0.001$) but was not significantly different than that of the nonadenomas ($p = 0.03$).

The mean enhancement, enhancement washout, and percentage enhancement washout were all significantly lower ($p < 0.001$) for the nonadenomas than for the adenomas.

The relative percentage enhancement washout of the lipid poor adenomas was significantly lower than that of the lipid-rich adenomas ($p < 0.001$). Nevertheless, the relative percentage enhancement washout was still significantly higher for lipid-poor adenomas than that of the nonadenomas ($p < 0.001$). The optimal threshold value of percentage enhancement washout for both lipid-poor and lipid-rich adenomas was 60%. For the relative percentage enhancement washout for lipid-poor adenomas, the optimal threshold was 40%.

Giovanni Foti retrospectively evaluated the accuracy of unenhanced attenuation and relative percentage wash-in ratio in early, - arterial and portal venous phase, biphasic CT in differentiating adrenal adenomas from metastatic lesions.

One hundred seven adrenal masses in 86 patients were evaluated. Diagnosis was achieved with percutaneous biopsy ($n = 6$), surgery ($n = 13$), and at least 1 year of imaging follow-up ($n = 88$). Unenhanced, arterial phase, and portal phase scans were obtained. Diameter and absolute attenuation values in each phase of CT were measured. Relative percentage wash-in ratio was calculated.

The final diagnosis was metastasis in 51 cases and adenoma in 56 cases. A significant difference was found between benign and malignant lesions in regard to diameter ($p = 0.001$), unenhanced CT attenuation ($p = 0.001$), and relative percentage wash-in ratio from the arterial to the portal venous scan ($p = 0.014$). In the differentiation of benign from malignant lesions, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of unenhanced CT attenuation (at an 11-HU threshold) were 98%, 86%, 86%, 98%, and 92%, and those of relative percentage wash-in ratio from the arterial to the portal venous phase were 94%, 77%, 79%, 93%, and 85%.

Boland et al reported that lipid-poor adrenal lesions, which contain a low lipid-to-water proton ratio, cannot generally be characterized by chemical shift methods, as their signal intensity is unchanged on opposed-phase images. These lesions are then considered indeterminate on the basis of chemical shift MR images.

B K Park et al retrospectively assessed adrenal incidentalomas detected by triphasic helical CT using modified relative percentage of the enhancement washout (mRPEW) values. 42 adrenal incidentalomas in 35 patients were detected on CT and confirmed by either pathological examination or follow-up CT examination. The mRPEW values were calculated using the attenuation values of the adrenal masses seen on the images from portal phase and delayed phase CT performed 3 min after intravenous injection of contrast material. The diagnostic accuracy of an adenoma was obtained using the mRPEW values. The final diagnosis was an ‘‘adenoma’’ and a ‘‘metastasis’’ in 9 and 33 cases, respectively. The mRPEW values of the adenomas and metastases ranged from 5.8% to 59.4% and from –18.8% to 25%, respectively (p,0.05). An mRPEW value of 20% yielded the best accuracy of 88% (37/42) for an adenoma. mRPEW values .25% and #5% had a positive predictive value of 100% (3/3) and a negative predictive value of 100% (15/15), respectively. They concluded that a substantial number of adrenal incidentalomas may be characterized using the mRPEW values from triphasic helical CT.

Sung-Woo Park et al attempted to resolve the dilemma regarding indeterminate adrenal lesions by assessing the relative percentage washout of adrenal lesions after contrast-enhanced CT. In a multicenter study, they determined the accurate cut-off value and delayed time of the washout rate for adrenal adenomas by final pathologic diagnosis. 244 patients undergoing adrenalectomies at 5 university hospitals in Pusan, Korea between 2005 and 2009 were reviewed. They calculated the mean value of Housfield units in residual lesions _ 3 times using the region of interest (ROI) during pre-operative non-enhancing CT scans, and early and delayed images in enhanced CT scans. We used ROC curves to determine the specificity and sensitivity of non-enhanced CT scans and the washout rate according to the diagnostic criteria for adrenal adenomas. They divided the patients into the following 2 groups:- adrenal adenoma group (n_138); and non-adrenal adenoma group (n_106). There was no significant difference in age, gender, and right and left findings between the two groups. Based on the ROC curves, the specificity and sensitivity was 45.7% and 97% for the non-enhancing CT scans (HU_10), and 93.9% and 95.8% for the 15-minute washout rate (_55%) respectively.

Constantino S. Peña et al determined whether computed tomographic (CT) scans and attenuation measurements on contrast material–enhanced and nonenhanced CT scans could be used to characterize adrenal masses, in particular, to characterize these lesions by using adrenal washout characteristics at contrast-enhanced CT. Eighty-six patients (49 men, 37 women; age range, 29–86 years; mean age, 72 years) with 101 adrenal lesions depicted at contrast-enhanced CT underwent delayed (mean, 9 minutes) enhanced scanning. Seventy-eight patients also underwent nonenhanced CT. Mean diameter of the benign lesions was 2.1 cm (range, 1.0–4.2 cm); mean diameter of the malignant lesions was 2.3 cm (range, 1.0–4.1 cm). Region-of-interest measurements were obtained at nonenhanced, dynamic enhanced, and delayed enhanced CT and were used to calculate a relative percentage washout as follows: 1 − (Hounsfield unit measurement on delayed image ÷ Hounsfield unit measurement on dynamic image) × 100%. Ninety-nine of 101 lesions were correctly characterized as benign or malignant with a relative percentage washout threshold of 50% on delayed scans; benign lesions demonstrated more than

50% washout; and malignant lesions, less than 50% washout. Two benign lesions demonstrating less than 50% washout were characterized as benign by using conventional CT. They concluded that calculation of relative percentage washout on dynamic and delayed enhanced CT scans may lead to a highly specific test for adrenal lesion characterization, reduce the need for, and possibly obviate, follow-up imaging or biopsy.

D H Szolar et al measured the changes in wash-in and washout of contrast material on contrast material-enhanced computed tomographic (CT) scans in patients with adrenal adenomas and nonadenomas. One hundred twenty-two patients with 135 adrenal masses (74 adenomas, 61 nonadenomas) underwent helical CT. Unenhanced CT was followed by enhanced CT at 30, 60, and 90 seconds and 3, 10, and 30 minutes. The adenomas enhanced significantly more than the nonadenomas at 60 seconds ($P < .001$), but the percentage enhancement of the adenomas was significantly greater than that of the nonadenomas at 30, 60, and 90 seconds ($P < .001$). At 3, 10, and 30 minutes, the absolute percentage loss of enhancement and the relative percentage loss of enhancement were significantly greater for the adenomas than for the nonadenomas ($P < .001$). Delayed enhanced CT at 10 minutes (sensitivity, 92%; specificity, 95%) and 30 minutes (sensitivity, 97%; specificity, 100%) was more accurate for differentiation of adenomas and nonadenomas than unenhanced CT (sensitivity, 82%; specificity, 95%). They concluded that adrenal adenomas exhibit greater washout of contrast material than do adrenal nonadenomas. The percentage change in washout of contrast material is a useful adjunct to absolute CT attenuation values in differentiation of adrenal adenomas and nonadenomas.

Takuro Kamiyama et al retrospectively examined the diagnostic values of individual parameters obtained from unenhanced and 35-second and 5-minute contrast material–enhanced (enhanced) computed tomography (CT) in distinguishing adenomas, particularly lipid-poor adenomas, from nonadenomas and to determine the best diagnostic method by using these parameters.

The study population consisted of 61 patients (20 men and 41 women; mean age, 58 years) with 68 adrenal masses (53 adenomas and 15 nonadenomas). In each patient, unenhanced CT was followed by 35-second and 5-minute enhanced CT. Adenomas were classified as 30 lipid-rich (_10 HU) and 23 lipid-poor (_10 HU) adenomas by using unenhanced attenuation. The diagnostic parameters were tumor size, unenhanced attenuation, 35-second and 5-minute enhanced attenuation, wash-in and washout attenuation, percentage enhancement washout ratio (PEW), and relative PEW (RPEW). The sensitivity, specificity, and accuracy for diagnosing adenomas were calculated by using a threshold level of each parameter determined by the least sum of false-positive and false-negative cases and a combination of the threshold levels with 100% specificity. The best results were obtained by using a combination of the threshold levels with 100% (15 of 15) specificity (presence of at least one of the following criteria for diagnosing adenomas: unenhanced attenuation of _19 HU, 5-minute attenuation of _50 HU, PEW of _45%, and RPEW of _31%). Sensitivity was 94% (50 of 53) or 87% (20 of 23) and accuracy was 96% (65 of 68) or 92% (35 of 38) for diagnosing total adrenal adenomas or lipid-poor adenomas, respectively.

They concluded that combining the diagnostic parameters of the CT protocol can yield diagnostic results comparable to those with previously reported longer dynamic enhanced CT protocols.

John K. Yoon et al reported a case of a 50 year old man for whom Adrenal CT was then performed, with unenhanced, 60-second enhanced, and 15- minute delayed imaging. The right adrenal nodule measured 2.0 × 1.9 cm in maximum axial dimensions. Region of interest measured 37 H on the unenhanced images, 127 H on the 60-second contrast enhanced images, and 62 H on the 15-minute delayed images, representing 72% absolute contrast enhancement washout. The patient underwent a laparoscopic right adrenalectomy 6 weeks later, and the diagnosis of right adrenal pheochromocytoma was pathologically confirmed. This case of an incidental pheochromocytoma showing contrast medium washout greater than 50% on delayed imaging reiterated the importance of performing a biochemical profile in any patient with an incidentally discovered adrenal mass, regardless of clinical signs and symptoms.

Materials
&
Methods

MATERIALS AND METHODS

STUDY POPULATION

The study group includes a total 50 Patients with 54 adrenal masses who have come to the Department of Radiology at Madras Medical College.

STUDY PLACE:

Barnard Institute of Radiology, Madras Medical College and Government General Hospital, Chennai

STUDY DESIGN:

Prospective Study

INCLUSION CRITERIA

Patients with adrenal masses, measuring more than 1cm, with Hounsfield Unit more than 10.

EXCLUSION CRITERIA

Pregnant women

Severe hypersensitivity or previous allergic reactions

Critically ill patients

Patients in renal failure

The study was approved by our institutional ethical committee, and informed consent was obtained from all the patients. The examinations were performed during the period from June 2009 to October 2011.

CT MACHINES USED IN THE STUDY

Philips Brilliance 64 Slice

Figure 6

Toshiba Asteion 4 Slice

Figure 7

DATA ACQUISITION

Adrenal masses were evaluated with an adrenal CT imaging protocol. The dedicated adrenal CT protocol consisted of initial densitometry of the mass on unenhanced CT scans. If the mass had an attenuation of 10 HU or less, it was assumed to be benign and the masses were excluded from the study. Thus, twenty masses with HU below 10 were excluded.

Two masses with grossly visible fatty components (less than or equal to _30 HU) were presumed to be myelolipomas and were excluded from the study. Ten additional masses were excluded because of inadequate follow-up.

A diagnosis was established in the final study group of 54 masses when histologic proof was obtained at surgery or percutaneous biopsy.

All patients with adrenal masses that had attenuation values greater than 10 HU at unenhanced imaging underwent enhanced CT imaging 60 seconds after intravenous administration of contrast material and then underwent delayed enhanced CT imaging at 15 minutes.

The scans were done with a Philips Brilliance 64 slice CT scanner or Toshiba Asteion 4 slice CT scanner. Enhancement washout percentages were calculated for these masses.

To diagnose an adrenal mass as an adenoma, we used the previously reported thresholds of 60% or higher for absolute percentage washout and 40% or higher for relative enhancement washout.

Parameters for the unenhanced and delayed enhanced examinations with the CT scanners were KVp (Peak KV) of 120 kVp, Slice Thickness of 2mm and Slice Interval of 5mm. Enhanced scans were obtained after intravenous injection of 40 mL of iohexol 350 (Omnipaque).

IMAGE ANALYSIS

CT attenuation values were measured by using a circular region of interest on images of the adrenal lesion in question. The region of interest covered at least one-half of the mass, excluding cystic, calcified, or necrotic regions. The edges of the adrenal lesion were avoided to prevent partial volume averaging.

The enhancement washout percentages were calculated with the following equation

CONTRAST WASHOUT FORMULAE

Contrast Washout

Absolute wash out

$$\frac{\text{Enhanced CT (HU)} - \text{Delayed CT (HU)}}{\text{Enhanced CT (HU)} - \text{Unenhanced CT (HU)}} \times 100\%$$

Relative wash out

$$\frac{\text{Enhanced CT (HU)} - \text{Delayed CT (HU)}}{\text{Enhanced CT (HU)}} \times 100\%$$

Figure 8

The maximal diameters and the right or left side locations of the adrenal masses were also recorded.

Statistical analysis of variance was undertaken to examine the significance of the differences between the adenomas and nonadenomas in terms of mean mass size, mean attenuation value at unenhanced CT, mean attenuation value at enhanced CT, mean attenuation value at delayed enhanced CT, mean percentage of enhancement washout, and mean relative percentage of enhancement washout.

A *p* value less than .05 was considered to indicate a statistically significant difference. The threshold values of 60% or higher for absolute percentage enhancement washout and 40% or higher for relative percentage enhancement washout used in the diagnosis of adenoma were established in prior investigations

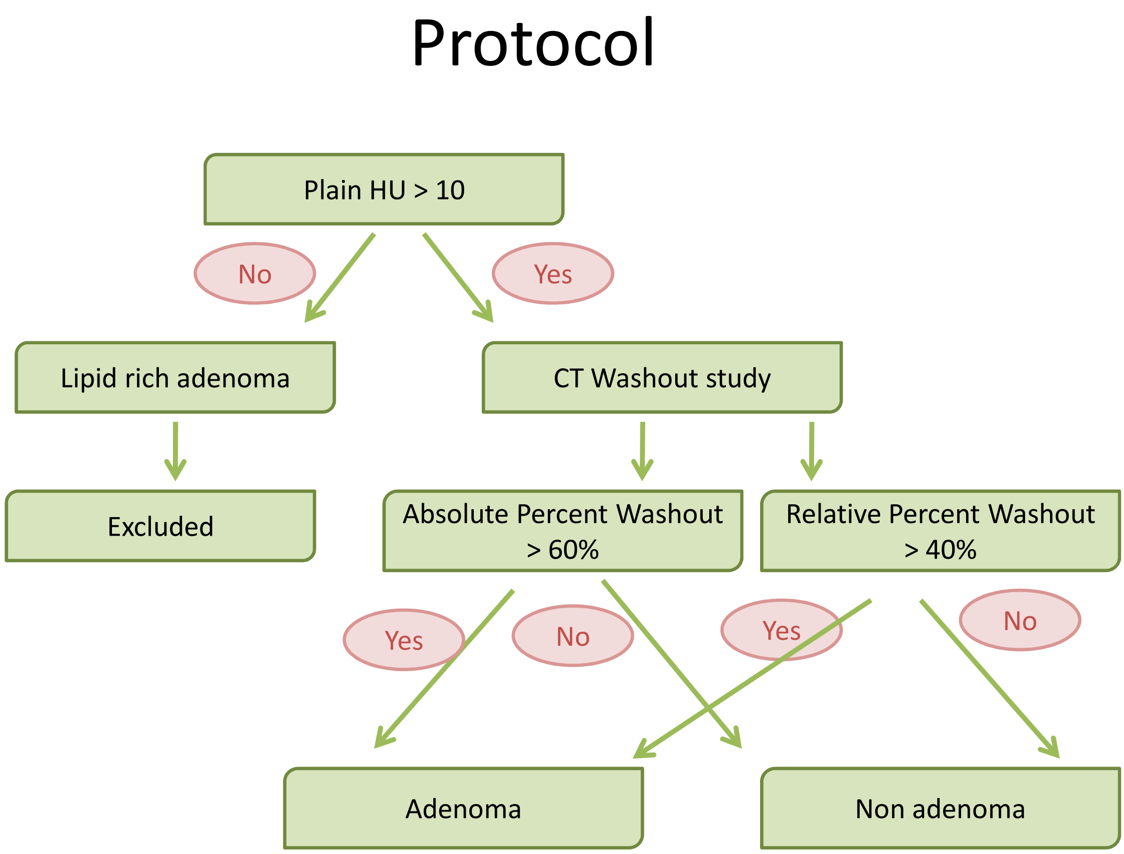

Protocol
Plain HU > 10
No
Yes
Lipid rich adenoma
CT Washout study
Excluded
Absolute Percent Washout > 60%
Relative Percent Washout > 40%
Yes
No
Yes
No
Adenoma
Non adenoma

Figure 9

Results
&
Statistical Analysis

RESULTS

Number:

The final clinical diagnosis was adrenal adenoma for 25 masses and nonadenoma for 29 masses, confirmed at pathologic examination.

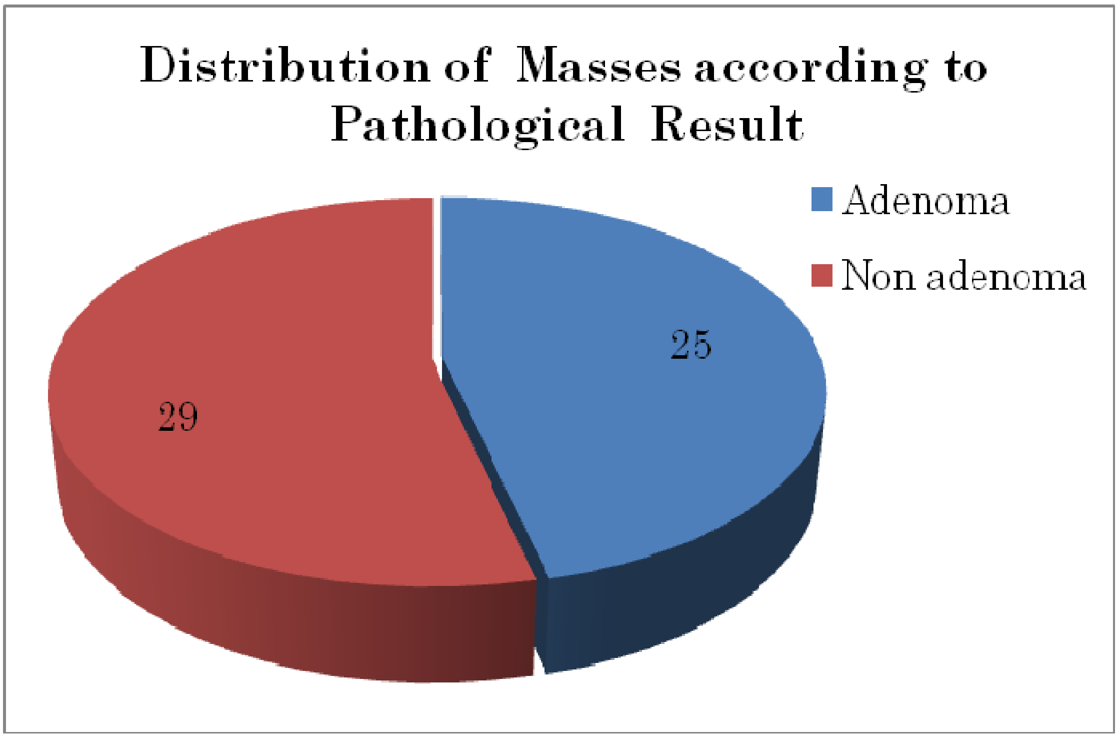


Figure 10

Side:

Adenomas were more often found in the right (n = 14) than in the left (n = 11) adrenal gland.

Nonadenomas were found in the left adrenal gland in 13 cases and in the right adrenal gland in 16 cases.

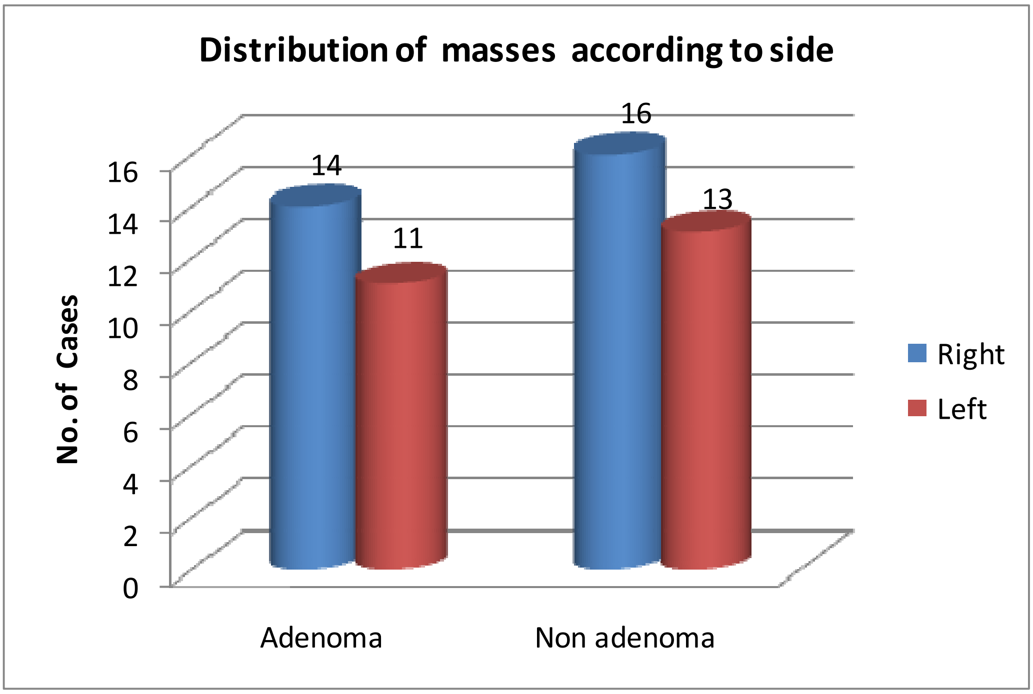


Figure 11

Sex:

The patient population with adrenal adenomas consisted of 11 women and 14 men with a mean age of 48 years (range, 23–73 years). In 1 of these patients, there were bilateral adrenal masses.

The patient population with nonadenomas consisted of 12 women and 17 men with a mean age of 55 years (range, 26–75 years). 2 patients had bilateral adrenal masses.

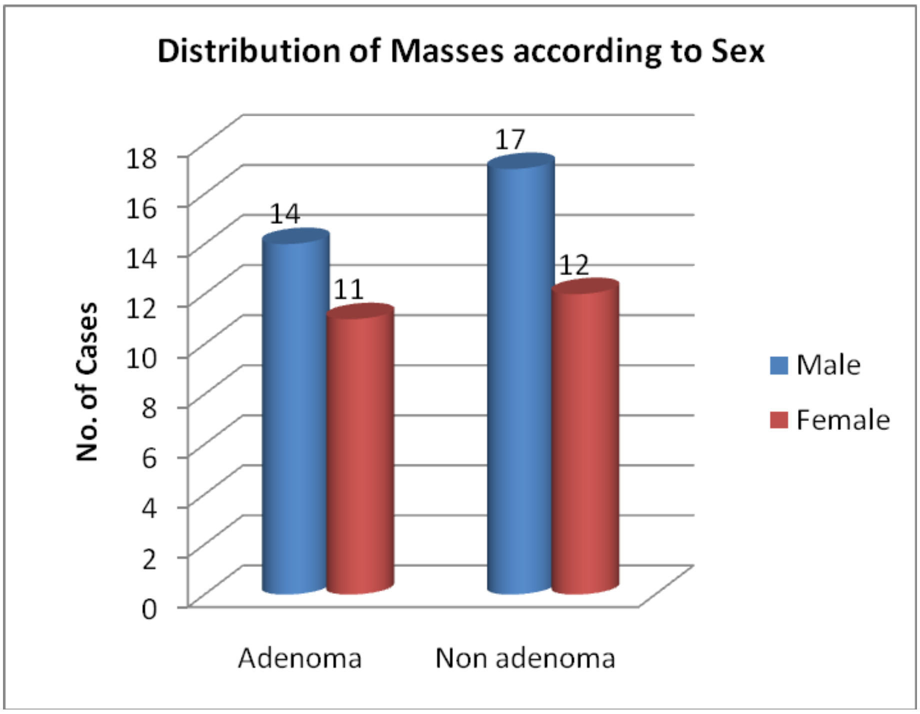


Figure 12

Size

The average maximal diameter of the adenomas was 3.5 cm (range, 2.5–5.1 cm, with Standard deviation of 0.6).

Nonadenomas were larger (mean size, 4.2 cm; range, 2.7–6.3 cm, with Standard deviation of 1.0). It was found to be statistically significant with a p value of 0.005.

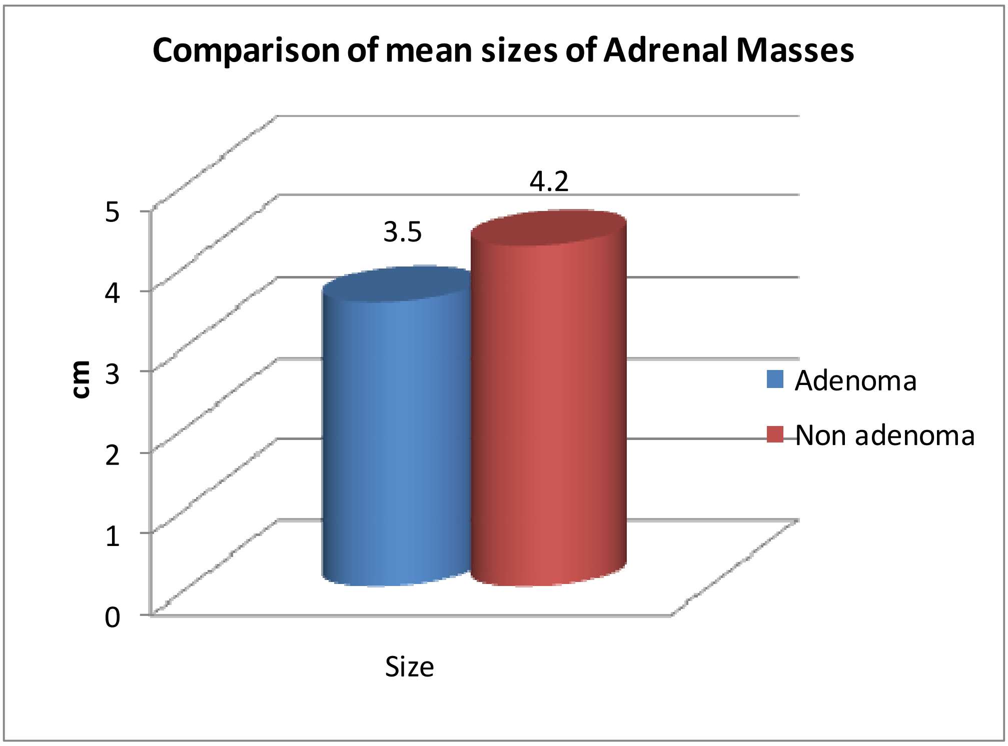


Figure 13

The mean attenuation values of adenomas and nonadenomas on unenhanced, enhanced, and delayed enhanced CT scans are shown in Table 1.

Table 1: **Mean attenuation values of Adrenal Masses**

	Unenhanced	**Enhanced**	**Delayed**
Adenoma	23.5	75.3	41.6
Non adenoma	27.2	66.2	45.9

The nonadenomas included 26 metastases, two pheochromocytomas, one adrenal cortical carcinoma.

The primary malignancies in the 26 patients who had adrenal metastases were the following: lung cancer (n =17), esophageal cancer (n = 2), renal cancer (n = 2), tongue cancer (n = 1), rectal cancer (n = 1) and breast cancer (n =3).

STATISTICAL ANALYSIS

Mean unenhanced attenuation value:

The mean unenhanced value of the adenomas (23.5 HU, with Standard deviation of 4.9) was significantly different from that of the non-adenomas (27.2 HU with Standard deviation of 1.0). The *p* value was 0.022).

Mean enhanced attenuation value:

The mean attenuation value of the adenomas at enhanced CT (75.3 HU with Standard deviation of 13.1) was significantly higher than that of the nonadenomas (66.2 HU with Standard deviation of 10.6). The *p* value was 0.007

Mean delayed attenuation value:

The mean attenuation value of the adenomas at delayed enhanced CT (41.5 HU with Standard deviation of 7.3) was lower than that of the nonadenomas (45.9 HU with Standard deviation of 8.8). The p value was 0.059, not found to be statistically significant.

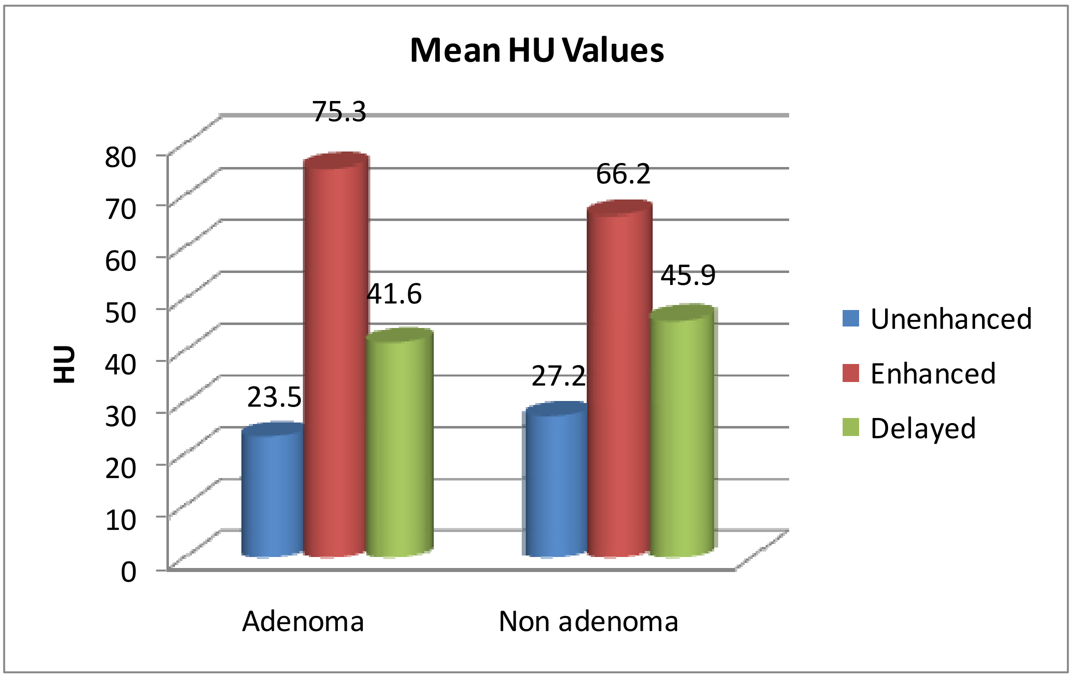


Figure 14

Scatterplots of HU values

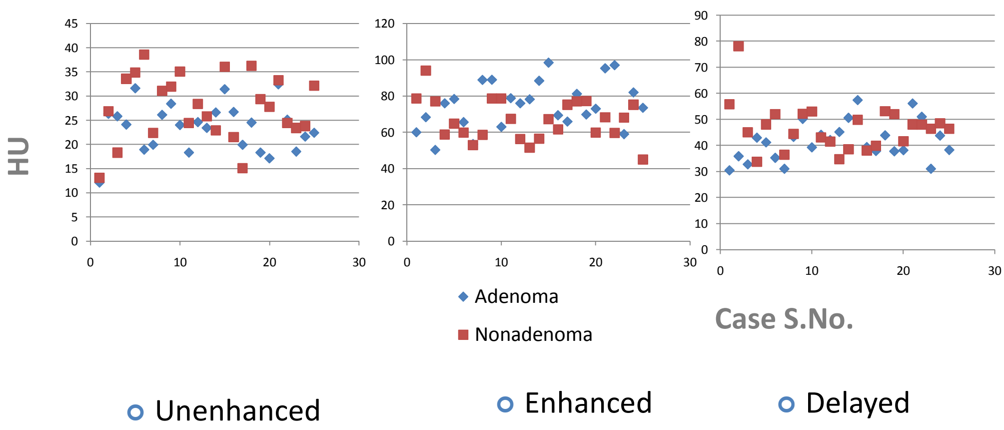


Figure 15

T-Test

Table 2 : Group Statistics

	Path Result	N	Mean	Std. Deviation	Std. Error Mean
Size	Adenoma	25	3.464	.6297	.1259
	Non-adenoma	29	4.159	1.0387	.1929
Plain	Adenoma	25	23.520	4.9086	.9817
	Non-adenoma	29	27.248	6.4066	1.1897
Enhanced	Adenoma	25	75.256	13.0951	2.6190
	Non-adenoma	29	66.210	10.6104	1.9703
Delayed	Adenoma	25	41.580	7.3367	1.4673
	Non-adenoma	29	45.879	8.8179	1.6374
Absolute washout	Adenoma	25	65.544	5.3920	1.0784
	Non-adenoma	29	54.441	11.8583	2.2020
Relative washout	Adenoma	25	44.616	3.6383	.7277
	Non-adenoma	29	30.645	7.0130	1.3023

Table 3 : Independent Samples Test

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
Size	-2.912	52	.005	-.695	.2385	-1.1733	-.2159
	-3.015	46.999	.004	-.695	.2304	-1.1581	-.2312
Plain	-2.370	52	.022	-3.728	1.5730	-6.8848	-.5718
	-2.417	51.342	.019	-3.728	1.5424	-6.8243	-.6322
Enhanced	2.804	52	.007	9.046	3.2265	2.5713	15.5200
	2.760	46.176	.008	9.046	3.2774	2.4493	15.6420
Delayed	-1.929	52	.059	-4.299	2.2291	-8.7723	.1737
	-1.955	51.945	.056	-4.299	2.1987	-8.7114	.1128
Absolute washout	4.309	52	.000	11.103	2.5766	5.9322	16.2730
	4.528	40.335	.000	11.103	2.4519	6.1484	16.0568
Relative washout	8.967	52	.000	13.971	1.5581	10.8447	17.0976
	9.365	43.290	.000	13.971	1.4918	10.9633	16.9791

Distribution of values

Although the means of the attenuation values at enhanced CT and the attenuation values at delayed enhanced CT for lipid-poor adenomas and nonadenomas were significantly different, there was too much overlap among the individual values of the two groups to permit differentiation between them for any individual mass.

Table 4: Mean Washout Percentages

	Absolute percent washout	**Relative percent washout**
Adenoma	65.5 %	44.6 %
Non adenoma	54.4 %	30.6 %

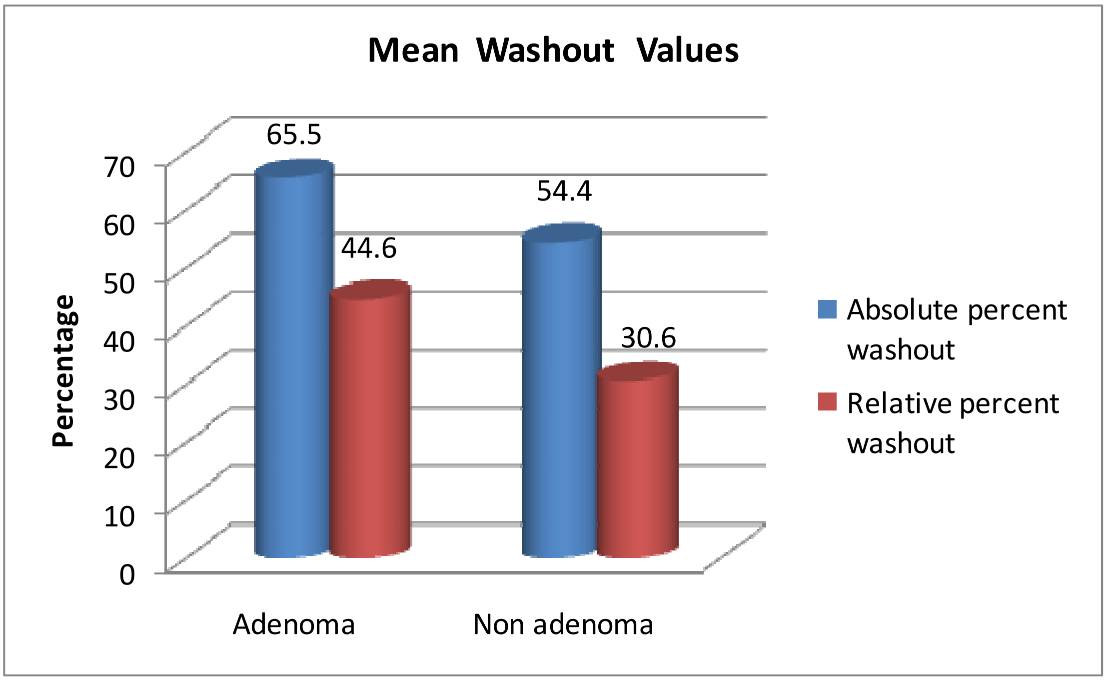


Figure 16

Scatterplots of Washout Values

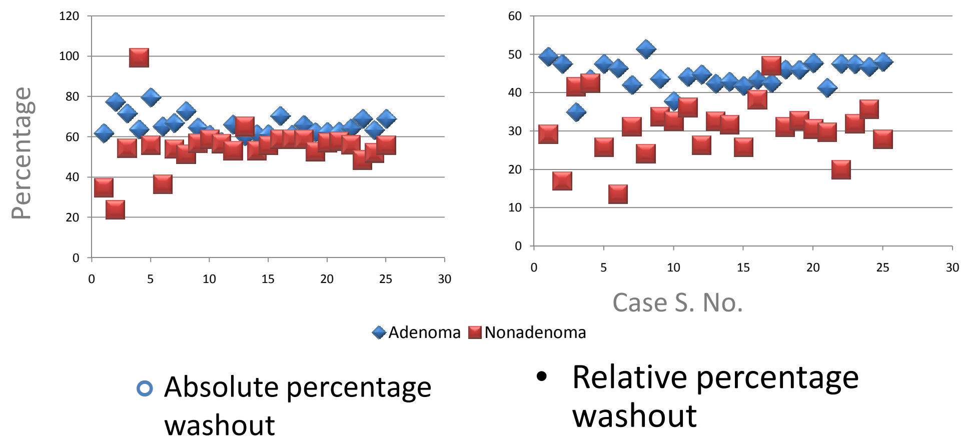


Figure 17

Absolute percentage enhancement washout:

The absolute percentage enhancement washout value of the adenomas (65.5% with Standard deviation of 5.4) was significantly higher than that of the nonadenomas (54.4% with Standard deviation of 11.9). The *p value was* <0.001**. (** - significance at 1% level)

Table 5: Result Absolute percentage washout * Pathological Result Crosstab

			Path Result		**Total**
			Adenoma	**Non-adenoma**	
Result Abs	Adenoma	Count	24	2	26
		% within Result Abs	92.3%	7.7%	100.0%
		% within Path Result	96.0%	6.9%	48.1%
	Non-adenoma	Count	1	27	28
		% within Result Abs	3.6%	96.4%	100.0%
		% within Path Result	4.0%	93.1%	51.9%
Total		Count	25	29	54
		% within Result Abs	46.3%	53.7%	100.0%
		% within Path Result	100.0%	100.0%	100.0%

Table 6 : Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	42.696 (b)	1	.000		
Continuity Correction(a)	39.202	1	.000		
Likelihood Ratio	51.833	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	41.906	1	.000		
N of Valid Cases	54				

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 12.04.

Relative percentage enhancement washout value:

The relative percentage enhancement washout value of the adenomas (Mean 44.6%, with Standard deviation of 3.6) was also significantly higher than that of the nonadenomas (30.6%, with Standard deviation of 7.0) The p value was <0.001**. (** - significance at 1% level)

Table 7: Result Relative percent washout * Pathological Result Crosstab

			Path Result		**Total**
			Adenoma	**Non-adenoma**	
Result Rel	Adenoma	Count	23	3	26
		% within Result Rel	88.5%	11.5%	100.0%
		% within Path Result	92.0%	10.3%	48.1%
	Non-adenoma	Count	2	26	28
		% within Result Rel	7.1%	92.9%	100.0%
		% within Path Result	8.0%	89.7%	51.9%
Total		Count	25	29	54
		% within Result Rel	46.3%	53.7%	100.0%
		% within Path Result	100.0%	100.0%	100.0%

Table 8 : Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	35.856(b)	1	.000		
Continuity Correction(a)	32.660	1	.000		
Likelihood Ratio	41.557	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	35.192	1	.000		
N of Valid Cases	54				

a Computed only for a 2x2 table

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 12.04.

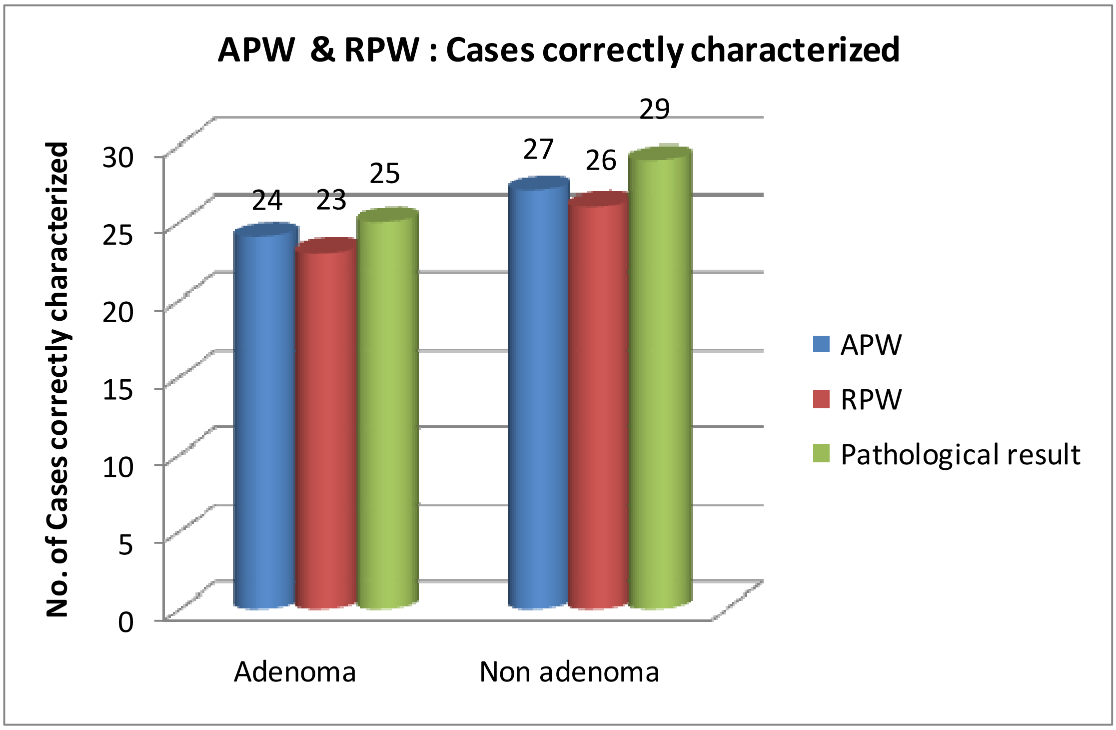

APW & RPW : Cases correctly characterized
No. of Cases correctly characterized
30
25
20
15
10
5
0
24
23
25
27
26
29
Adenoma
Non adenoma
APW
RPW
Pathological result

Figure 18

Absolute percent washout

The use of a threshold of 60% in the differentiation of adenomas from nonadenomas resulted in a sensitivity of 96% (24 of 25 masses) and a specificity of 93% (27 of 29 masses)

Table 9 : APW Outcome vs Pathological Result

	Adenoma	**Non adenoma**
Test + ve	24	2
Test –ve	1	27

APW > 60% ⇨ Test + ve ⇨ Adenoma

APW < 60% ⇨ Test - ve ⇨ Non adenoma

Table 10 : Statistical Evaluation of Absolute Percent Washout

Sensitivity	96.00%
Specificity	93.10%
PPV	92.31%
NPV	96.43%

There was 1 adenoma that did not meet the 60% threshold. The percentage enhancement washout measurements for this mass was 57.4%

Two nonadenomas had absolute percentage enhancement washout measurements above the 60% threshold. These washout measurements were 99.2% and 65.1%. Both were metastases.

Relative percent washout

The use of a relative percentage enhancement washout threshold value of 40% in the differentiation of the adenomas resulted in a sensitivity of 92% (23 of 25 masses) and a specificity of 89.66% (26 of 29 masses).

Table 11 : RPW Outcome vs Pathological Result

	Adenoma	Non adenoma
Test + ve	23	3
Test –ve	2	26

RPW > 40% ⇨ Test + ve ⇨ Adenoma

RPW < 40% ⇨ Test - ve ⇨ Non adenoma

Table 12 : Statistical Evaluation of Relative Percent Washout

Sensitivity	92.00%
Specificity	89.66%
PPV	88.46%
NPV	92.86%

The relative percentage enhancement washout measurements for the 2 adenomas that did not meet the 40% relative percentage enhancement threshold were 37.7%, 34.9%.1adenoma did not meet either threshold criteria.

3 Non adenomas were wrongly characterised with relative percent washout. The relative percentage enhancement washout measurements for these masses were 41.5%, 42.4% and 47% respectively.

Table 13 APW & RPW

	Sensitivity	**Specificity**
APW	96.00 %	93.1 %
RPW	92.00 %	89.66 %

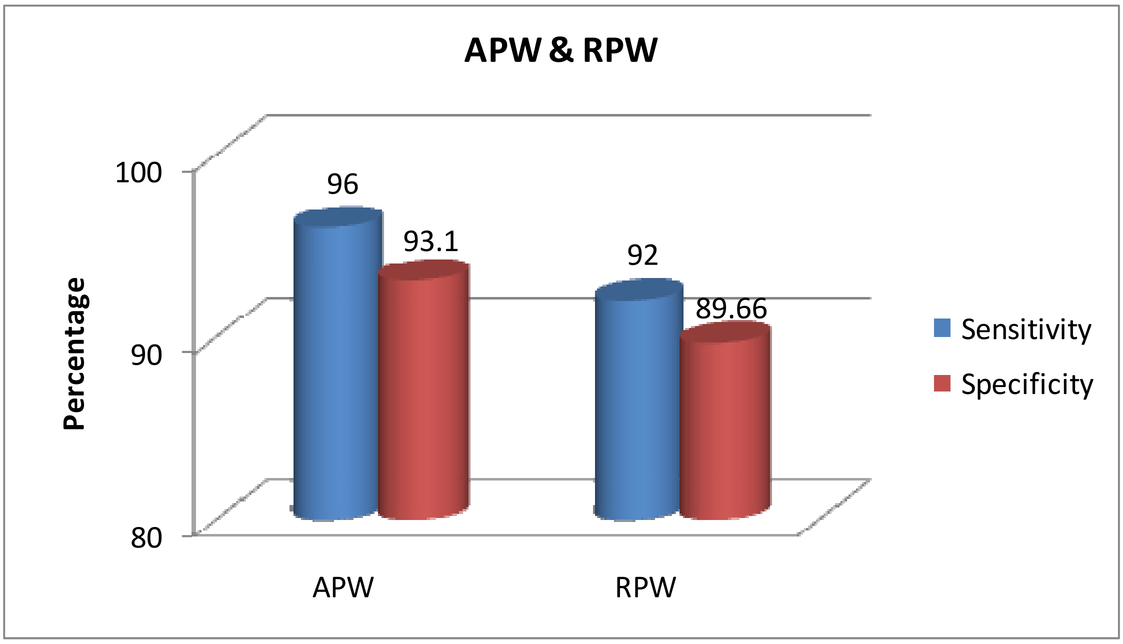


Figure 19

Discussion

DISCUSSION

In patients with a known extraadrenal primary neoplasm, differentiation of an adenoma from a metastasis is the principal reason an adrenal mass is characterized.

Nonadenomas such as pheochromocytomas and primary adrenal malignancies are rare, and the former can usually be diagnosed by virtue of their clinical and biochemical features.

There are two independent properties of adrenal adenomas that can be exploited in characterizing them at CT.

First, most adenomas contain large amounts of intracellular lipid, resulting in lower attenuation values at unenhanced CT than nonadenomas.

Second, all adenomas, including those without substantial lipid content, tend to have a more rapid loss of attenuation value soon after enhancement with intravenous contrast material.

The purpose of this study was to assess the accuracy, sensitivity and specificity of this method.

Absolute percentage enhancement washout threshold of 60% correctly diagnosed 24 of 25 adenomas. This was with a sensitivity of

96%, specificity of 93.1%. The positive and negative predictive values were 92.3% and 96.4% respectively.

Absolute percentage washout failed to correctly characterise two non adenomas. These included a metastasis from lung cancer and an incidentally detected metastasis. The values were 99.2% and 65.1% respectively.

It also failed to characterise 1 adenoma. This was in a patient with a lung primary, which it ruled as non adenoma. The value was 57.4%

Relative percent washout correctly characterised 23 of 25 adenomas and 26 of 29 non adenomas. The sensitivity and specificity were 92% and 89.7% respectively. The positive and negative predictive values were 88.5% and 92.7% respectively.

Relative percentage washout failed to correctly characterise three non adenomas. These included a metastasis from lung cancer and two incidentally detected metastases. The values were 41.5%, 47% and 42.4% respectively.

It also failed to characterise 2 adenomas. These included patients with an incidentally detected adenoma and a case of Cushing's syndrome which was also pathologically proven to be an adenoma. Both of them were characterised as non adenomas. The value was 34.9% and 37.7% respectively.

The ability of unenhanced CT densitometry to help diagnose adrenal adenomas has been extensively studied. A number of these investigations established that adenomas consistently have lower attenuation values than nonadenomas.

The amount of intratumoral lipid content of resected adrenal adenomas has directly correlated with a lower attenuation value at unenhanced CT.

Thus threshold of 10 HU on unenhanced CT images was used as a cutoff for the inclusion criteria.

Based on previous studies conducted on adrenal masses and their unenhanced attenuation values, it has been established that masses with very low unenhanced attenuation values are adenomas with high sensitivity and specificity. Thus a mass that is 10 HU or less on unenhanced CT images is diagnosed radiologically as an adenoma and a CT contrast washout study is not undertaken.

Based on the attenuation values at unenhanced, enhanced and delayed enhanced CT and calculations of absolute and relative percentage enhancement washouts, adenomas demonstrate a greater percentage of enhancement washout compared with nonadenomas.

The results of this study confirms those of prior studies and demonstrates that the mean attenuation values at unenhanced CT adrenal adenomas and those of nonadenomas are nearly identical.

Although the two groups have significantly different mean attenuation values at both enhanced and delayed enhanced CT, the considerable overlap between the two groups is too large to permit sufficiently accurate differentiation between them for any individual case.

The distribution of the enhancement washout calculations for the two groups, however, was significantly different to allow accurate differentiation of individual cases.

Absolute percent washout correctly characterised 51 of 54 adrenal masses with an accuracy of 94.44%

Relative percent washout correctly characterised 49 of 54 adrenal masses with an accuracy of 90.74%

The relative enhancement washout value is an approximation of the true enhancement washout value; it relates the decrease in attenuation value on delayed enhanced images to the initial enhanced value, instead of to the difference between the enhanced and the unenhanced values.

Absolute enhancement washout values were more accurate than use of the relative enhancement washout value in the differentiation of adenomas from nonadenomas.

LIMITATIONS OF THE STUDY

Only 50 patients and 54 adrenal masses were included in the study. This patient population may be small. This results are to be considered preliminary and in need of further evaluation. Future studies involving large patient groups may be helpful to determine the usefulness of this technique for specific adrenal lesions.

The study did not include masses with unenhanced attenuation values less than 10HU. Although previous studies have established that masses below 10HU are adenomas, there may be a few cases that could be exceptions.

Third, partial volume averaging errors could have been made in the measurements of smaller masses. This may have falsely lowered or raised the recorded attenuation values.

Conclusion

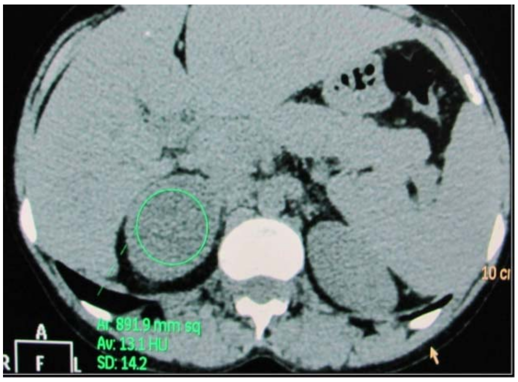
CONCLUSION

Adenomas can be differentiated from nonadenomas at delayed enhanced CT examinations with absolute and relative percentage enhancement washout calculations.

This protocol enables nearly all adrenal masses to be diagnosed with a high sensitivity and specificity.

Thus CT contrast washout study for adrenal masses plays a definitive role in guiding clinical management.

CASE 1



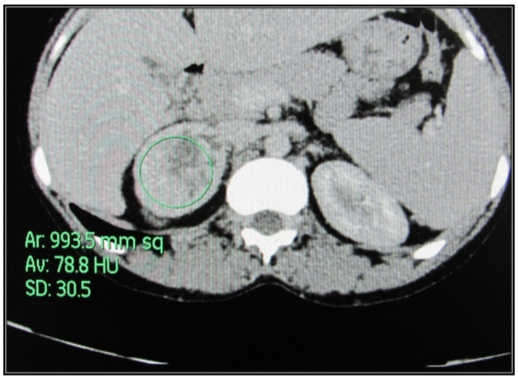


Fig 20a : **Plain - HU 13.1**

*Fig 20b:***Enhanced - HU 78.8**

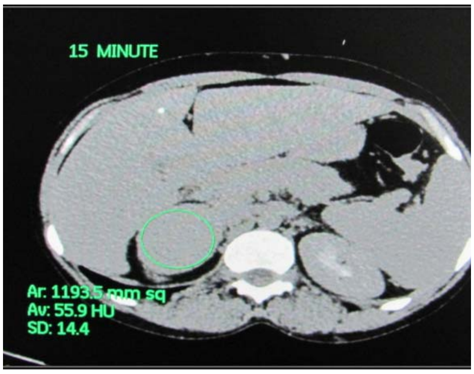


*Fig 20c :***Delayed – HU 55.9**

Absolute Percent Washout	34.9	Non adenoma	Correct
Relative Percent Washout	29.1	Non adenoma	Correct
Pathological Diagnosis	Metastasis	Non adenoma	

CASE 2

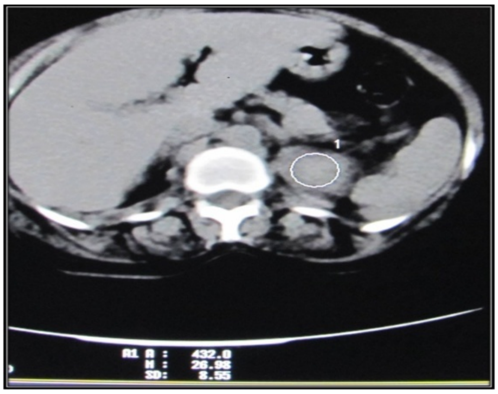


Fig 21a: **Plain - HU 26.9**

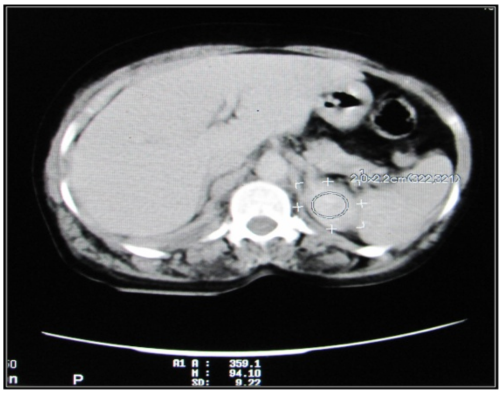


*Fig 21b:***Enhanced - HU 94.1**

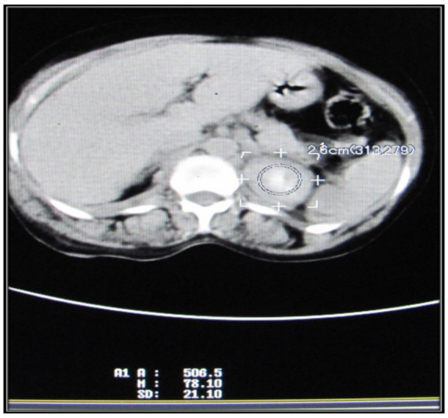


Fig 21c : **Delayed – HU 78.1**

Absolute Percent Washout	23.8	Non adenoma	Correct
Relative Percent Washout	17.0	Non adenoma	Correct
Pathological Diagnosis	Metastasis	Non adenoma	

CASE 3

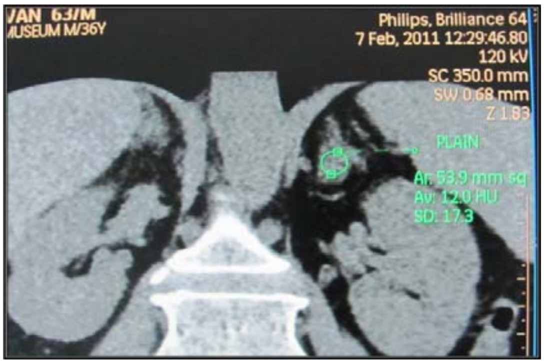


Fig 22a : **Plain - HU 12**

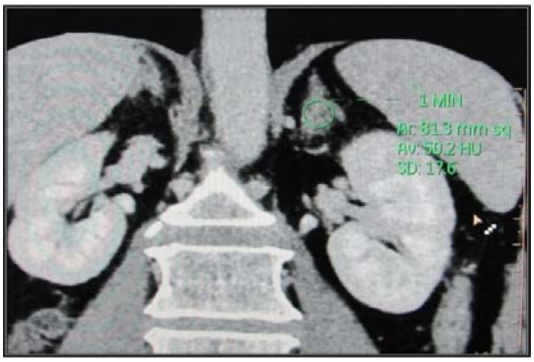


Fig 22b: **Enhanced - HU 22.3**

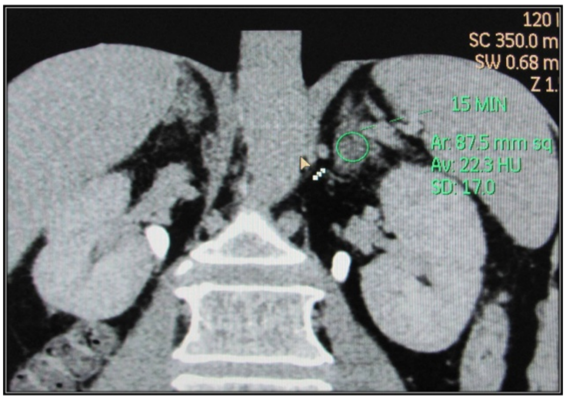
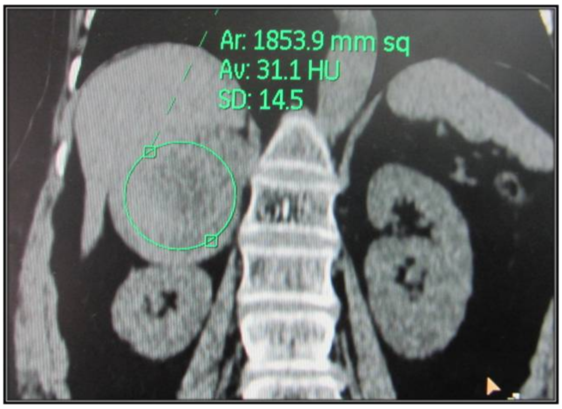


Fig 22c : **Delayed – HU 50.2**

Absolute Percent Washout	73.0	Adenoma	Correct
Relative Percent Washout	55.6	Adenoma	Correct
Pathological Diagnosis	Adenoma	Adenoma	

CASE 4



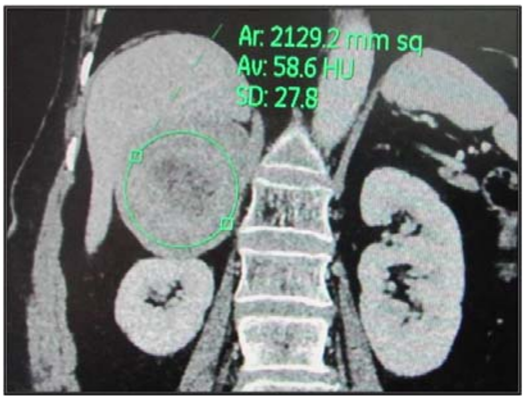


Fig 23a **: Plain - HU 31.1** ***Fig 23b :*** **Enhanced - HU 58.6**

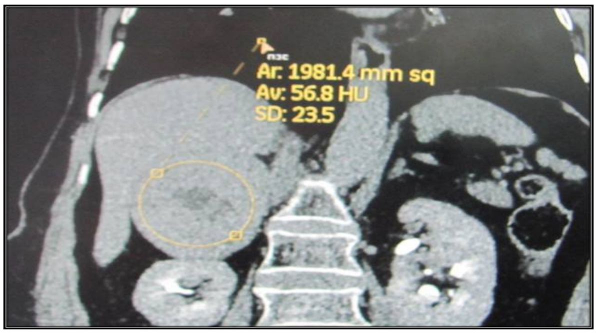


Fig 23c : **Delayed – HU 56.8**

Absolute Percent Washout	6.5	Non adenoma	Correct
Relative Percent Washout	3.1	Non adenoma	Correct
Pathological Diagnosis	Adrenocortical carcinoma	Non adenoma	

CASE 5

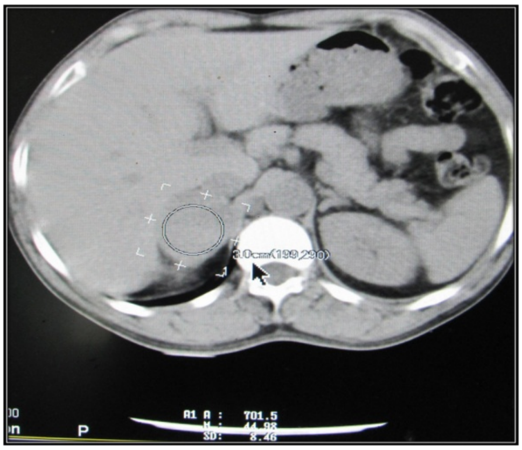


Fig 24a: **Plain - HU 44.9**

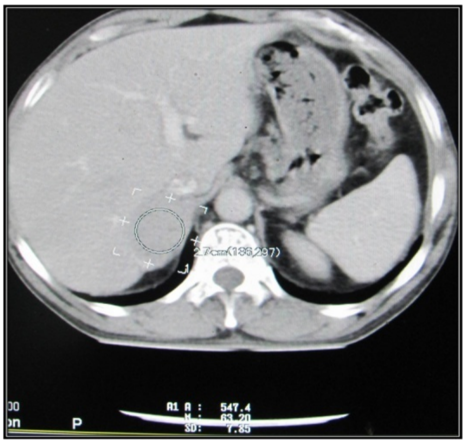


Fig 24b : **Enhanced - HU 63.2**

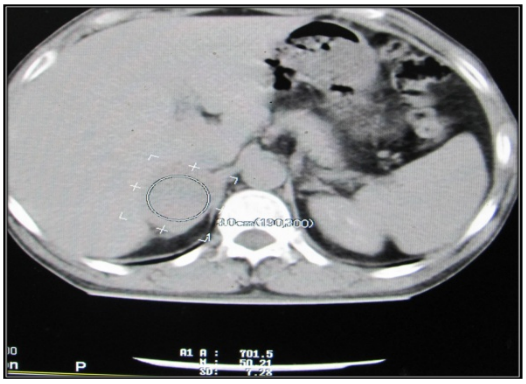


Fig 24c : **Delayed – HU 50.2**

Absolute Percent Washout	71.0	Adenoma	Incorrect
Relative Percent Washout	20.6	Non adenoma	Correct
Pathological Diagnosis	Pheochromocytoma	Non adenoma	

CASE 6

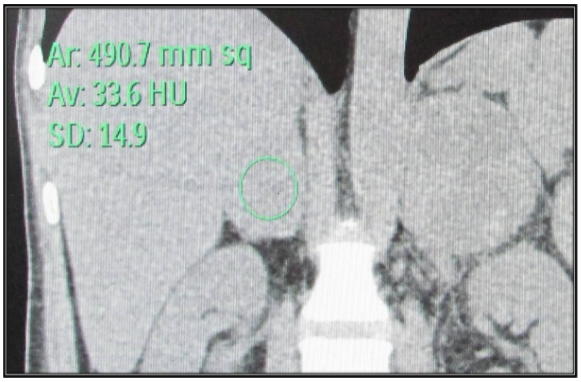


Fig 25a : **Plain - HU 33.6**

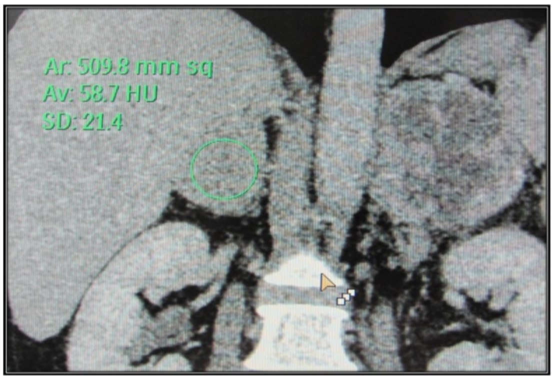


Fig 25b: **Enhanced - HU 58.7**

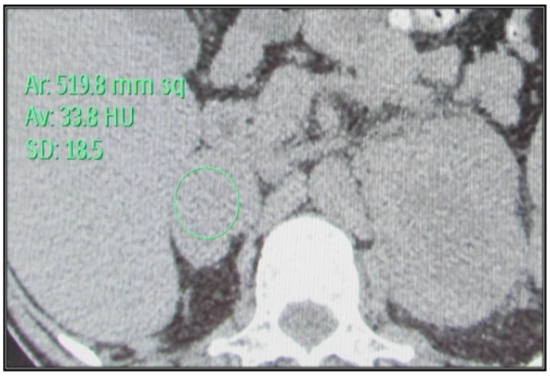


Fig 25c: **Delayed – HU 33.8**

Absolute Percent Washout	99.2	Adenoma	Incorrect
Relative Percent Washout	42.4	Adenoma	Incorrect
Pathological Diagnosis	Metastasis	Non adenoma	

Bibliography

BIBLIOGRAPHY

1. Al-Hawary MM, Francis IR & Korobkin M 2005 Noninvasive evaluation of the incidentally detected indeterminate adrenal mass. Tumour Biology 19 277–292.

2. Bae KT, Fuangtharnthip P, Prasad SR, Joe BN, Heiken JP. Adrenal masses: CT characterization with histogram analysis method. Radiology 2003;228:735–742.

3. Bertherat J, Mosnier-Pudar H & Bertagna X 2002 Adrenal incidentalomas. Current Opinion in Oncology 14 58–63.

4. Benitah N, Yeh BM, Qayyum A. Minor morphologic abnormalities of adrenal glands at CT: prognostic importance in patients with lung cancer. Radiology 2005;235:517–522.

5. Blake MA, Kalra MK, Sweeney AT, et al. Distinguishing benign from malignant adrenal masses: multi-detector row CT protocol with 10-minute delay. Radiology 2005;238: 578–585.

6. Blake MA, Krisnamoorthy SK, Boland GW, et al. Low density pheochromocytoma on CT: a mimicker of adrenal adenoma. AJR Am J Roentgenol 2003;181:1663–1668.

7. Boland GW, Lee MJ, Gazelle GS, Halpern EF, McNicholas MMJ, Mueller PR. Characterization of adrenal masses using unenhanced

CT: an analysis of the CT literature. AJR Am J Roentgenol 1998; 171: 201–204.

8. Boland GW, Hahn PF, Pena C, Mueller PR. Adrenal masses: characterization with delayed contrast-enhanced CT. Radiology 1997; 202:693–696

9. Bovio S, Cataldi A, Reimondo G, et al. Prevalence of adrenal incidentaloma in a contemporary computerized tomography series. J Endocrinol Invest 2006;29:298– 302.

10. Caoili EM, Korobkin M, Francis IR, Cohan RH, Platt JF, Dunnick NR & Raghupathi KI 2002 Adrenal masses: Characterization with combined unenhanced and delayedenhanced CT. Radiology 222 629–633.

11. Dunnick NR & Korobkin M 2002 Imaging of adrenal incidentalomas: current status. American Journal of Roentgenology 179 559–568.

12. Fajardo R, Montalvo J, Velazquez D, Arch J, Bezaury P, Gamino R & Herrera MF 2004 Correlation between radiologic and pathologic dimensions of adrenal masses. World Journal of Surgery 28 494–497.

13. Fogel J, Blake MA, Kalra MK, et al. A 10- minute CT protocol for differentiating benign from malignant adrenal masses [letter] Radiology 2007;242:947–948.

14. Francis IR, Glazer GM, Shapiro B, Sisson JC, Gross BH. Complementary roles of CT and 131I-MIBG scintigraphy in diagnosing pheochromocytoma. AJR Am J Roentgenol 1983;141:719–725.

15. Grumbach MM, Biller BM, Braunstein GD, Campbell KK, Carney JA, Godley PA, Harris EL, Lee JK, Oertel YC, Posner MC et al. 2003 Management of the clinically inapparent adrenal mass ('incidentaloma'). Annals of Internal Medicine 138 424–429.

16. Hamrahian AH, Ioachimescu AG, Remer EM, Motta- Ramirez G, Bogabathina H, Levin HS, Reddy S, Gill IS, Siperstein A & Bravo EL 2005 Clinical utility of noncontrast computed tomography attenuation value (hounsfield units) to differentiate adrenal adenomas/ hyperplasias from nonadenomas: cleveland clinic experience. Journal of Clinical Endocrinology and Metabolism 90 871–877.

17. Heinz-Peer G, Memarsadeghi M & Niederle B 2007 Imaging of adrenal masses. Current Opinion in Urology 17 32–38.

18. Ilias I, Alesci A & Pacak K 2004 Current views on imaging of adrenal tumours. Hormone and Metabolic Research 36 430–435.

19. Korobkin M, Giordano TJ, Brodeur FJ, Francis IR, Siegelman ES, Quint LE, Dunnick NR, Heiken JP & Wang HH 1996 Adrenal adenomas: relationship between histologic lipid and CT and MR findings. Radiology 200 743–747.

20. Korobkin M, Brodeur FJ, Francis IR, Quint LE, Dunnick NR & Londy F 1998 CT time-attenuation washout curves ofadrenal adenomas and nonadenomas. American Journal of Roentgenology 170 747–752.

21. Korobkin M, Francis IR, Kloos RT, Dunnick NR. The incidental adrenal mass. Radiol Clin North Am 1996; 34:1037–1054.

22. Lam KY, Lo CY. Metastatic tumors of the adrenal glands: a 30-year experience in a teaching hospital. Clin Endocrinol (Oxf) 2002;56:95–101.

23. Lee MJ, Hahn PF, Papanicolau N, et al. Benign and malignant adrenal masses: CT distinction with attenuation coefficients, size, and observer analysis. Radiology 1991; 179:415–418.

24. Lerttumnongtum P, Muttarak M, Visrutaratna P & Ya-In C 2004 Imaging features of unusual adrenal masses. Australasian Radiology 48 107–113.

25. Lingam RK, Sohaib SA, Rockall AG, Isidori AM, Chew S, Monson JP, Grossman A, Besser GM & Reznek RH 2004 Diagnostic

performance of CT versus MR in detecting aldosterone-producing adenoma in primary hyperaldosteronism (Conn’s syndrome). European Radiology 14 1787–1792.

26. LockhartME, Smith JK& Kenney PJ 2002 Imaging of adrenal masses. European Journal of Radiology 41 95–112.

27. Mantero F, Terzolo M, ArnaldiG,OsellaG,MasiniAM, AliA, Giovagnetti M, Opocher G & Angeli A 2000 A survey on adrenal incidentaloma in Italy Study Group on Adrenal Tumours of the Italian Society of Endocrinology. Journal of Clinical Endocrinology and Metabolism 85 637–644.

28. Outwater EK, Siegelman ES, Huang AB, Birnbaum BA. Adrenal masses: correlation between CT attenuation value and chemical shift ratio at MR imaging with in-phase and opposed-phase sequences. Radiology 1996; 200:749–752.

29. Park BK, Kim CK, Kim B, Lee JH. Comparison of delayed enhanced CT and chemical shift MR for evaluating hyperattenuating incidental adrenal masses. Radiology 2007; 243:760–765.

30. Pena CS, Boland GW, Hahn PF, Lee MJ, Mueller PR. Characterization of indeterminate (lipid-poor) adrenal masses: use of washout characteristics at contrast-enhanced CT. Radiology 2000;217:798–802.

31. Rockall AG, Babar SA, Sohaib SA, Isidori AM, Diaz-Cano S, Monson JP, Grossman AB & Reznek RH 2004 CT and MR imaging of the adrenal glands in ACTH-independent Cushing syndrome. Radiographics 24 435–452.

32. Sahdev A & Reznek RH 2004 Imaging evaluation of the non-functioning indeterminate adrenal mass. Trends in Endocrinology and Metabolism 15 271–276.

33. Slattery JM, Blake MA, Kalra MK, Misdraji J, Sweeney AT, Copeland PM, Mueller PR & Boland GW 2006 Adrenocortical carcinoma: contrast washout characteristics on CT. American Journal of Roentgenology 187 W21–W24.

34. Sohaib SA, Hanson JA, Newell-Price JD, Trainer PJ, Monson JP, Grossman AB, Besser GM & Reznek RH 1999 CT Appearance of the adrenal glands in adrenocorticotrophic hormone-dependent Cushing's syndrome. American Journal of Roentgenology 172 997–1002.

35. Sohaib SAA, Bomanji J, Evanson J & Reznek RH 2001 Imaging of the endocrine system. Grainger & Allison's Diagnostic Radiology – A Textbook of Medical Imaging, pp 1367–1399. Eds RG Grainger, DJ Allison, A Adam & AK Dixon., 5 London: Churchill Livingstone

36. Song JH, Chaudhry FS, Mayo-Smith WW. The incidental indeterminate adrenal mass on CT: prevalence of adrenal disease in 1,049 consecutive adrenal masses in patients with no known malignancy. AJR Am J Roentgenol 2008;190:1163–1168.

37. Szolar DH, Korobkin M, Reittner P, Berghold A, Bauernhofer T, Trummer H, Schoellnast H, Preidler KW & Samonigg H 2005 Adrenocortical carcinomas and adrenal pheochromocytomas: mass and enhancement loss evaluation at delayed contrast-enhanced CT. Radiology 234 479–485.

38. Thompson GB & Young WF Jr 2003 Adrenal incidentaloma. Current Opinion in Oncology 15 84–90.

39. Vincent JM, Morrison ID, Armstrong P & Reznek RH 1994. The size of normal adrenal glands on computed tomography. Clinical Radiology 49 453–455 (Erratum Clin Radiol Vol. 50 (1995) 202)

40. Young WF Jr 2007 The incidentally discovered adrenal mass. New England Journal of Medicine 356 601–610.

Annexures

PROFORMA

"CHARACTERIZATION OF ADRENAL MASSES WITH CONTRAST ENHANCED CT"

Sl.No: Date:

Name: IP No:

Age/Sex:

Occupation:

Address:

Presenting Complaints

		Yes	**No**
Abdominal Pain	:		
Abdominal mass	:		
Loss of Appetite	:		
Loss of weight	:		
Cough	:		
Hemoptysis	:		
Hametemesis	:		
Haematuria	:		
Others	:		

Past History

H/O similar episodes before -

H/O Abdominal surgery -

Others -

Vital signs

Pulse -

BP -

Respiratory rate -

Examination of Abdomen

Abdomen tenderness -

Abdomen mass -

Others -

Lab finding

Complete blood profile -

Blood glucose -

Blood urea -

Creatinine -

Other -

Chest X ray findings:

Baseline USG findings

CT Chest findings (if taken)

MRI Abdomen & PET scan (if taken)

CECT Abdomen findings

Side of adrenal mass	:
Size	:
Attenuation value in Plain CT	:
Attenuation value in Contrast CT 1 minute study	:
Attenuation value in Contrast CT 15 minute study	:
Absolute washout ratio	:
Relative washout ratio	:
Adenoma/ /Non adenoma	:

HPE findings

ABBREVIATIONS

P	–	Unenhanced HU Value
E	–	Enhanced HU Value
D	–	Delayed HU Value
APW	–	Absolute Percentage Washout
RPW	–	Relative Percentage Washout
R APW Washout	–	Result based on Absolute Percentage
R RPW Washout	–	Result based on Relative Percentage
Path	–	Histopathological Result

MASTER CHART

S no	Patient	Age	Sex	History	Side	Size	P	E	D	APW	RPW	R APW	R RPW	Path
1	Sathya	29	F	Incidental	R	3.1	13.1	78.8	55.9	34.8	29.1	NA	NA	NA
2	Meena	60	F	Lung mass	R	3.2	26.9	94.1	78.1	23.8	17	NA	NA	NA
3	Thuravudeen	50	M	Hypertension	L	3.3	18.3	77.1	45.1	54.4	41.5	NA	A	NA
4	Chandrasekar	48	M	Lung mass	R	4.1	33.6	58.7	33.8	99.2	42.4	A	A	NA
5	Perumal	65	M	Lung mass	R	6.3	34.9	64.8	48.1	55.8	25.8	NA	NA	NA
6	Perumal	65	M	Lung mass	L	4.5	38.6	59.9	52.1	36.6	13.6	NA	NA	NA
7	Kesavan	63	M	Abd pain	L	3.4	12.1	60.1	30.5	61.7	49.3	A	A	A
8	Chinnakannu	45	M	Incidental	R	3.7	22.4	53	36.5	53.9	31.1	NA	NA	NA
9	Pattu	70	F	Renal mass	R	5.9	31.1	58.6	44.5	51.3	24.1	NA	NA	NA
10	Mariammal	40	F	Incidental	R	3.7	26.3	68.4	35.9	77.2	47.5	A	A	A
11	Jagadeesan	69	M	Abd pain	L	4.7	32	78.7	52.2	56.7	33.7	NA	NA	NA
12	Jeeva	36	M	Hypertension	L	3.8	25.8	50.4	32.8	71.5	34.9	A	NA	A
13	Raniammal	58	F	Colon cancer	R	4	24.1	76.1	43	63.6	43.5	A	A	A
14	Sivaraman	35	M	Abd pain	R	2.8	31.6	78.5	41.2	79.5	47.5	A	A	A
15	Govindammal	72	F	Bone mets	L	3.1	35.1	78.7	53.1	58.7	32.5	NA	NA	NA
16	Pasupathy	67	M	Lung mass	R	2.5	18.9	65.7	35.3	65	46.3	A	A	A
17	Pushpa	42	F	Incidental	L	3.1	24.4	67.5	43.1	56.6	36.1	NA	NA	NA
18	Palani	59	M	Liver metastasis	R	3.2	19.9	53.6	31.1	66.8	42	A	A	A
19	Peter	57	M	Liver metastasis	L	5.1	28.4	56.3	41.5	53	26.3	NA	NA	NA
20	Helen	68	F	Lung mass	R	3.3	26.1	89	43.3	72.7	51.3	A	A	A

S no	Patient	Age	Sex	History	Side	Size	P	E	D	APW	RPW	R APW	R RPW	Path
21	Xavier	55	M	Incidental	L	3.4	25.8	51.6	34.8	65.1	32.5	A	NA	NA
22	Xavier	55	M	Incidental	R	3.4	28.4	89.1	50.2	64.6	43.6	A	A	A
23	Fathima	62	F	Lung secondaries	R	3.1	22.9	56.4	38.6	53.1	31.6	NA	NA	NA
24	Chandrasekar	48	M	Lung mass	L	4.3	36.1	67.2	49.9	55.6	25.7	NA	NA	NA
25	Annammal	56	F	Lung mass	R	3.6	21.5	61.6	38.1	58.6	38.1	NA	NA	NA
26	Vadivel	46	M	Incidental	L	4.6	15.1	75.3	39.9	58.8	47	NA	A	NA
27	Munirathnam	29	M	Cushing's	R	3.5	24	63.1	39.3	60.9	37.7	A	NA	A
28	Banumathy	28	F	Hypertension	R	5.1	36.3	77.1	53.2	58.6	31	NA	NA	NA
29	Nambirajan	57	M	Lung mass	L	3.7	18.3	78.9	44.1	57.4	44.1	NA	A	A
30	Suseela	61	F	Lung mass	L	3.5	24.6	76.1	42.1	66	44.7	A	A	A
31	Dawood	67	M	Incidental	R	6.1	29.4	77.3	52.1	52.6	32.6	NA	NA	NA
32	Arockiamary	69	F	Renal mass	R	3.2	27.8	59.9	41.6	57	30.5	NA	NA	NA
33	Dhanasekar	61	M	Lung mass	R	2.7	23.4	78.3	45.2	60.3	42.3	A	A	A
34	Kasiamma	46	F	Lung secondaries	L	2.8	26.6	88.5	50.6	61.2	42.8	A	A	A
35	Zahirabanu	36	F	Pelvic pain	L	3	31.4	98.5	57.4	61.2	41.7	A	A	A
36	Francis	71	M	Incidental	R	4.4	33.3	68.3	48.1	57.7	29.6	NA	NA	NA
37	Ezhilarasu	49	M	Incidental	L	3.7	24.4	59.6	48	55.9	19.9	NA	NA	NA
38	Ponnamma	75	F	Lung mass	R	2.7	23.4	68.1	46.4	48.5	31.9	NA	NA	NA
39	Muthuvelu	71	M	Lung mass	L	3.3	26.7	69.5	39.4	70.3	43.3	A	A	A
40	Ramasamy	57	M	Lung secondaries	R	2.9	23.8	75.3	48.5	52	35.6	NA	NA	NA
41	Seetha	34	F	Incidental	R	4.1	19.9	66	37.9	60.9	42.5	A	A	A

S no	Patient	Age	Sex	History	Side	Size	P	E	D	APW	RPW	R APW	R RPW	Path
42	Valarmathi	50	F	Lung mass	L	4.1	24.5	81.3	43.9	65.8	46	A	A	A
43	Veerasamy	45	M	Incidental	L	4.9	32.2	64.3	46.4	55.8	27.8	NA	NA	NA
44	Dhayalan	24	M	Incidental	R	3.4	18.3	69.9	37.8	62.2	45.9	A	A	A
45	Lakshmi	58	F	Lung mass	R	5.1	17.1	73.1	38.2	62.3	47.7	A	A	A
46	Ponnuthai	73	F	Bone mets	L	3.8	32.4	95.4	56.1	62.4	41.2	A	A	A
47	Radhammal	26	F	Hypertension	L	5.7	21.1	45.4	32.1	54.7	29.2	NA	NA	NA
48	Manickam	61	M	Incidental	R	5.2	26.3	67.2	45.2	53.8	32.7	NA	NA	NA
49	Muthu	23	M	Incidental	L	4.7	25.1	97.1	51	64	47.5	A	A	A
50	Samundi	32	M	Abd pain	R	2.5	18.5	59.1	31.1	68.9	47.4	A	A	A
51	Samundi	32	M	Abd pain	L	3.2	21.6	82.1	43.8	63.3	46.7	A	A	A
52	Feroz	57		Abd pain	R	3.7	27.5	60.3	42.2	55.2	30	NA	NA	NA
53	Srija	29	F	Incidental	R	3.1	22.4	73.6	38.3	68.9	48	A	A	A
54	Susaiammal	61	F	Incidental	L	3.9	24.5	59	41.4	51	29.8	NA	NA	NA

<u>ஆராய்ச்சி ஒப்புதல் கடிதம்</u>

ஆராய்ச்சி தலைப்பு

அதிரனற் சுரப்பி கட்டிகளை சி.டி. ஸ்கேன் கான்ட்ராஸ்ட் மூலமாக வகைப்படுத்தும் ஆய்வு

பெயர்	:	தேதி	:
வயது	:	உள் நோயாளி எண்	:
பால்	:	ஆராய்ச்சி சேர்க்கை எண்	:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கமும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் தான் பங்கு கொள்கிறேன் மற்றும் இந்த ஆராய்ச்சியில் இருந்து எந்நேரமும் பின் வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.

எனக்கு இந்த ஆராய்ச்சி குறித்த விவரங்கள் அடங்கிய தகவல்தாளினைப் பெற்றுக்கொண்டேன்.

எனக்கு கதிர்வீச்சு சிகிச்சை மற்றும் மருந்து சிகிச்சை முடிந்த பிறகு அறுவை சிகிச்சை செய்து கொள்ள சம்மதம் தெரிவிக்கிறேன்.

கதிர்வீச்சு சிகிச்சை மற்றும் மருந்து சிகிச்சை மற்றும் அறுவை சிகிச்சைக்கு தேவையான சிறப்பு மருத்துவ பரிசோதனைகள் செய்து கொள்ள சம்மதம் தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியின் மூலம் ஏற்படும் பக்கவிளைவுகள் அனைத்தும், மருத்துவரால் எனக்கு புரியும்படி விளக்கப்பட்டது.

நான் என்னுடைய சுயநினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

கையொப்பம்

தேதி

Title: CHARACTERIZATION OF ADRENAL MASSES WITH CONTRAST ENHANCED CT – WASHOUT STUDY

Authors: Dr.R.Shankaranandh

Coauthors : Prof.Dr.K.Vanitha, Prof.N.Kailasanathan, Prof.R.Malathy, Prof.S.Kalpana, Prof.S.Babu Peter, Prof.D.Ramesh, Dr.S.Sundareswaran, Dr.J.Devimeenal, Dr.Manimekala, Dr.J.Chezhian, Dr.K.Geetha

Institution: Barnard Institute of Radiology, Madras Medical College.

Aim of the study: To prospectively characterize adrenal masses as adenomas or non adenomas with Contrast enhanced CT and correlate with histopathological results

Materials & Methods: Fifty four adrenal masses were evaluated. CT attenuation values were measured using a circular region of interest on images of the lesion, covering at least one half of the mass. Adrenal masses that had attenuation values greater than 10 HU at unenhanced imaging underwent enhanced CT imaging 60 seconds after intravenous administration of contrast material and then underwent delayed enhanced CT imaging at 15 minutes. Enhancement washout percentages were calculated with the following equations:

Absolute percentage of enhancement washout:
([Attenuation value at enhanced CT - Attenuation value at delayed enhanced CT]/ [Attenuation value at enhanced CT - Attenuation value at unenhanced CT]) * 100.

Relative percentage of enhancement washout:
([Attenuation value at enhanced CT - Attenuation value at delayed enhanced CT]/ Attenuation value at enhanced CT) * 100.

An adenoma was diagnosed if a mass had an absolute percentage enhancement washout value of 60% or higher or relative percentage enhancement washout value of 40% or higher.

Results: The pathological diagnosis was 25 adenomas and 29 non adenomas. Absolute percent washout diagnosed 24 of 25 adenomas and 27 of 29 non adenomas. It had a Sensitivity of 96.00%, Specificity of 93.10%, Positive Predictive Value of 92.31% and Negative Predictive Value of 96.43%. Relative percent washout diagnosed 23 of 25 adenomas and 26 of 29 non adenomas. It had a sensitivity of 92%, specificity of 89.66%, Positive Predictive value of 88.46% and Negative Predictive Value of 92.86%. Both were found to be statistically significant.

Conclusion. CT contrast washout study is helpful in categorising adenomas and non adenomas in adrenal masses with high degree of accuracy, sensitivity and specificity and helps guide clinical management.